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National Institutes of Health

DIVISION OF RESEARCH RESOURCES

ANNUAL REPORT

FISCAL YEAR 1981

(October 1, 1980 - September 30, 1981)

National Institutes of Health
Bethesda, Md. 20205

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MISSION:

Identifies and meets the research resource needs and opportunities of the NIH by conceiving, creating, developing, and assuring the availability of those resources that are essential for the efficient and effective conduct of human health research.

Helps institutions establish and operate general clinical research centers where research studies can be conducted on patients over a wide range of human diseases; supports highly sophisticated biotechnology resources, such as computer centers, high voltage electron microscopy centers, and biological structure determination centers; supports primate research centers; increases and improves laboratory animal facilities and resources; makes awards for minority biomedical support, and provides institutional research support for stabilizing and developmental efforts among a variety of institutions throughout the United States.

Provides a unified approach to solving the many complex needs of health-oriented research that tends to be institutional, regional, or national in scale.

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REPORT OF THE DIRECTOR

Dr. James F. O'Donnell
Acting Director
Division of Research Resources

I. Report of the Acting Director

Fiscal Year (FY) 1981 brought significant changes to the Division of Research Resources (DRR) with respect to leadership and organizational goals. Having served most ably for over a decade as the Director, DRR, Dr. Thomas G. Bowery, in December 1980, requested of Dr. Donald S. Fredrickson, Director, NIH, that he be permitted to step down and assume a program role within the DRR. Dr. Fredrickson consented to the reassignment and on January 12, 1981, Dr. Bowery assumed the role of Director, Biomedical Research Support (BRS) Program. Dr. James F. O'Donnell, Deputy Director, was appointed Acting Director of the Division and Dr. Francis J. Kendrick, formerly Director of the BRS Program, became the Assistant Director for Manpower and Resource Development.

In December 1980, the vacancy in the Directorship of the Animal Resources Program, occasioned by the retirement of Dr. Charles McPherson, was filled by Dr. William I. Gay.

At the February 1981 meeting of the National Advisory Research Resources Council Dr. Fredrickson announced that prior to establishing a Search Committee for a new Director of DRR, he wished to examine the broad NIH activities, both DRR Programs and others, which he termed "communal resources," in light of the needs and constraints for the NIH biomedical research effort of the 1980s. He enlisted the Council's assistance, and after meeting with them again at the May 1981 meeting, the Council and DRR top staff developed a preliminary design for a National Research Resources Program. The plan was delivered to Dr. Fredrickson on June 18, 1981, one day before Dr. Fredrickson announced that he was retiring from the position of Director, NIH.

Final design and implementation of the activities encompassed in the plan for a National Research Resources Program have been held in abeyance with Dr. Fredrickson's departure. The Acting Director, NIH, Dr. Thomas E. Malone, has encouraged us to begin assembling data relating to the impact of DRR Programs on NIH activities and the research community. He has also established a Search Committee to select candidates for the position of Director, DRR. The final selection will be made by the new Director, NIH, when that position is filled.

An activity closely relating to our interests in expanding the data base of NIH research resources is the Research Resources Coordinating Committee (RRCC). Moving into its second year of activity, the RRCC began to intensify its exploration of NIH's enterprise of research resources by planning to deal with issues on a longer-range basis, and developing new mechanisms for solving associated problems. Information gathering and exchange were more extensive and covered a broader range of topics. The Committee resorted to various subgroups, advisory committees, and special review committees in order to experiment with and establish new ways to decide about the organizational location, the magnitude of funding, and maintenance of the vitality of different kinds of research resources.

Decisions were made to resolve crisis funding situations and other concerns for such resources as the Laboratory Animal Data Bank of the National Library of Medicine, the Kurland Epidemiology Data Bank supported by the National Institute of General Medical Sciences (NIGMS), and core grants supported by a number of

NIH Institutes. A new technical/conceptual review practice was successfully carried out for the Chemical Information System of the National Heart, Lung, and Blood Institute and the American Type Culture Collection managed by DRR, both of which are funded from the General Expense Fund of NIH. Many other resource program initiatives and issues were dealt with during the year, including the need for animal facilities improvement, the Shared Instrument Grant Programs of DRR and NIGMS, the Regional Medical Library Network, a national data bank for nucleic acids, and the development of an NIH-wide compendium on substances and living materials. The RRCC has taken steps recently to re-examine its role and will be seeking to achieve a number of objectives in the upcoming year. These will include the determination of needs for research resources, the setting of priorities, and the enlargement of its sphere of communication and participation.

In FY 1981, the Division began a comprehensive, systematic effort intended to produce program performance data on all the Division's Programs and major subprograms for use in future program management and planning activities. During March 1981, the managers of all the Division's Programs and major subprograms documented their Programs' objectives and developed indicators of their performance. After clearance and concurrence with the objectives and indicators by the Office of the Director, DRR, and the Office of the Director, NIH, program performance summaries are to be developed for all Programs, using the agreed-upon objectives and indicators as the starting points. Building on the program performance summaries, short-term evaluations will be performed for all the Division's Programs and major subprograms in FY 1982. The program performance summaries developed during FY 1981 will be enlarged during this activity to include FY 1982 results.

The Study, Evaluation of the Role of Clinical Research Centers and Clinical Trials, With Emphasis on Information Processing, (DRR 77-2), was completed in November 1980. The first phase of this Study was completed with the preparation, in December 1979, of an interim report characterizing clinical trials supported by NIH, both within the General Clinical Research Centers (GCRCs) and by the other Institutes. The Study then went on to examine the organizational, administrative, operational, and information-processing needs of the clinical trials carried out on and between the GCRCs to determine whether the Centers are providing an optimal environment for these trials. The final versions of both the interim and final reports were received by the Division in April 1981. The findings and recommendations of the Study are being reviewed by the Program and will be included in future Division planning.

The DRR review function was formally organized into a separate operation with the establishment of the Office of the Assistant Director for Review on July 1, 1980. This organization allows effective coordination of all review-related activities within the Division and has resulted in a greater separation of program and review functions. In FY 1980, primary emphasis was placed on developing standardized procedures and policies applicable to all DRR reviews.

Each of the Division's four committees has review responsibilities. They are the Animal Resources Review Committee which is composed of the Subcommittee on Animal Resources and the Subcommittee on Primate Research Centers; the Biotechnology Resources Review Committee, with its PROPHET Review Subcommittee; the General Clinical Research Centers Committee; and the General Research Support

Review Committee, with its Minority Biomedical Support Subcommittee and Biomedical Research Support Subcommittee. Although Biotechnology Resources grant applications are reviewed by the Division of Research Grants (DRG), the Biotechnology Resources Review Committee evaluates prospectuses submitted for access to the PROPHET Computer System.

During FY 1981, DRR review staff conducted initial reviews of 177 grant applications involving 97 project site visits.

With substantially increasing travel expenses, optional approaches to initial review were explored that did not include project site visits. One was the telephone conference call. A formal committee meeting was held using this process and included the review of seven grant applications. All discussions and voting were done over the telephone with priority scores and votes recorded on voting sheets and mailed to review staff, along with individual review reports after the meeting.

Another process used involved separating each of the individual research projects from their parent grant applications and assembling them according to various scientific areas. Individual panels were convened that consisted of individuals with the appropriate expertise for each scientific area and the projects were assigned to panels accordingly for scientific and technical merit review, a process similar to that conducted by a DRG Study Section. The applications were then reassembled and reviewed by the Program review committee.

Both mechanisms are considered to be suitable for the review of certain types of grant applications and should be useful options in the future.

Applications to the Biotechnology Resources Program continue to be reviewed by DRG. During this past year, close liaison was maintained with DRG. The previous practice of using the project site visit committee as the initial review committee for each application was discontinued. All site visits are now conducted separately with the findings and recommendations documented in individual reports and then forwarded to a Special Review Group, whose membership is represented on each site visit. This Committee completes the initial review by evaluating all applications at one meeting. The result has been higher quality and much more consistency among the reviews, especially in addressing issues unique to the Biotechnology Resources Program.

The Equal Employment Opportunity Committee of DRR planned and held a self-effectiveness workshop for DRR employees. The workshop participants met on four consecutive Wednesdays in the autumn and explored topics including effective and ineffective behavior patterns, sensitivity to the needs and rights of fellow workers, and methods for improving self-effectiveness. The Committee also participated in the "Career Options for the 80's Workshop" which focused on upward mobility and increased awareness of employee opportunities, and the Committee sponsored a series of informational luncheon meetings throughout the year.

In furtherance of the DRR mission, the Office of Administrative Management expanded its support for program planning and analysis by (1) streamlining its procedures for collecting data from the 1980 Annual Reports of Programs. These data were entered into the DRR information system by student summer employees. The data will be available for analysis and reports in the fall of 1981. (2) Two new subsystems were developed--one is for the data gleaned by the BRS Grant Annual Reports, and the second is a system which will provide very readable information to administrators in the NIH Institutes about their grantees' uses of DRR resources.

A joint project shared by Data Management and Financial Management staffs will result in a computerized system for monitoring the use of full-time equivalent (FTE) hours of employment. This computerized system will provide the needed position management control in FY 1982 and will complement the system currently under development by the NIH.

Major efforts were undertaken to implement the Employee Performance Management System, a methodology for planning and appraising the performance of DRR employees. Similarly, the second year of administering the Merit Pay System and the Senior Executive System within DRR continued. DRR's Personnel staff developed a Program which was well received to honor secretaries during National Secretaries Week, and at which the first annual award to an outstanding DRR secretary was presented. The same staff provided career counseling, not only to DRR employees, but to students and faculty members attending the annual Minority Biomedical Support Symposium.

Other major activities within the Office of the Director centered in the Office of Science and Health Reports (OSHR).

In 1976, OSHR established the Research Resources Information Center (RRIC) to promote the awareness of, the value of, the utilization of, and the access to DRR-supported research resources. Since that time, the Information Officer has offered technical guidance to the Center in order to help it expand its services.

During the fiscal year, the RRIC continued to extend its publications coverage. The circulation of the Reporter rose from 17,000 monthly at the beginning of the fiscal year to 22,000 at the end. Individual requests added to the mailing list averaged approximately 300 every month, and newstand distribution climbed from 5,000 copies per month to 7,000. There are 16 Reporter newstands on the NIH campus and at associated NIH office buildings in Bethesda, as well as in GCRCs in San Diego, San Francisco, and Torrance, California.

Although the Reporter is the monthly mainstay of the RRIC, during the year the Center completed the research, writing, and editing of several special reports with OSHR assistance: "CARTOS" (computer-aided reconstruction and tracing of serial sections) is a 16-page booklet with 10 illustrations that detailed the system which can visually reconstruct neural pathways; the second report was the 32-page "DRR 1980 Program Highlights," a compendium of Division information that included 38 photos and 6 figures.

In addition to the two special reports, the Center also produced during the fiscal year:

Minority Biomedical Support Directory (4th edition)
General Clinical Research Center Directory (3rd edition)

Biotechnology Resources Directory (4th edition)
Animal Resources Directory (4th edition--in press)

All resource directories were extensively revised based on the latest information from grantees as compiled through questionnaires and personal telephone contact.

The Division's publications, produced through the RRIC, continued to be recognized by awards from national organizations:

The "Seeds of Artificial Intelligence: SUMEX-AIM" was awarded first prize for brochures in national competition sponsored by the Health Sciences Communications Association (HeSCA).

The award, presented at the HeSCA annual meeting in May in Philadelphia, is the third for the publication. Previously, the booklet won first prize among technical publications in the National Association of Government Communicators 1980 competition and special recognition in the 1980 annual competition of the American Medical Writers Association, D.C. Chapter.

Earlier in the fiscal year, the American Academy of Pediatrics (AAP) gave its 1980 first-place award for magazine articles to "Anorexia Nervosa Studied at Several Centers," which appeared in the May 1980 issue of the Research Resources Reporter. The award cited the article for "distinguished achievement in pediatric journalism." The prize-winning piece covered research in GCRCs on the contributing and causative factors of the illness, which seems to affect primarily middle-class females.

In addition to the HeSCA and AAP awards, there was recognition for the booklet "1979 Program Highlights--Division of Research Resources." It received honorable mention in the "Other Serials" category at the 19th annual Blue Pencil Awards Program sponsored by the National Association of Government Communicators in Washington.

Through Columbia University, the site of the Biotechnology Resources grant involved, the Center produced a 15-minute film on the CARTOS neuron-tracing system. Information about the film was circulated to medical school faculty throughout the nation, together with copies of the CARTOS booklet. The second phase of the promotion was targeted to officers of neurological and related societies and associations. It asked that they publish an announcement of the film's availability from the RRIC in their publications.

Numerous Reporter articles were reprinted in other publications during the year, through the placement efforts of OSHR. Among the "recycled" pieces, placed by OSHR, after being slightly reworked, were:

Medical Tribune (January 14, 1981) Diaphragm Pacemaker
NIH News and Features (January 1981) Women's Hot Flashes
Medical Tribune (February 11, 1981) Plasmapheresis
Spectrum--CF Foundation (February 1981) Hypogammaglobulinemia
Children Today (January-February 1981) Infant Milk Allergy
NIH Search for Health (March 1981) Cooked Beef Flavor
JAMA (March 6, 1981) Fatal Genetics Disease Therapy

NIH News and Features (March 1981) Alcohol and Sex
Medical Tribune (March 11, 1981) Human Growth Hormone (Part 1)
Medical Tribune (March 18, 1981) Human Growth Hormone (Part 2)
Medical Tribune (April 1, 1981) Human Growth Hormone (Part 3)
Therapaeia (April 21, 1981) Shock Trauma
JAMA (May 1, 1981) Sucrose Polyester
Medical Tribune (May 27, 1981) Chronic Pain

A unique opportunity for the Reporter arose at Pennsylvannia State University. A professor of biochemistry wrote that he was revamping the University basic science course for non-science undergraduates. He felt today's student wanted to know what was going on in the biomedical field, but did not want to become involved in "minutia." In order to make a "relevant, interesting, solid, and comprehensible course for the non-science student," he requested copies of each Reporter issue which would serve as the basic text for the course. He promised the Center an evaluation of the revised course and its new "text."

Interest in Reporter reprints continued strong. The human growth hormone story in the December 1980 issue was distributed by the National Pituitary Agency and the Human Growth Foundation. The Professor of Medicine at Emory University and Director of the Hospital's Clinical Research Center, whose research was featured in the article, wrote: "Your article on growth hormone research was excellent . . . Please send us some copies as we would like to use it here for teaching purposes."

The Principal Investigator of the chimpanzee "language" studies and their application to retarded children wrote for 500 copies of the Reporter reprint.

During the year, with the cooperation and encouragement of the Project Officer, the RRIC converted all volume mailings of Center products to presorted, third-class bulk mail. The back cover format of all publications was redesigned to permit direct address labeling. This conversion is expected to save $125,000 a year in mailing costs.

An index for four years of the Reporter, from January 1977 to December 1980, was being completed as the fiscal year drew to a close. This index will be available to Reporter subscribers early in FY 1982.

In addition to its oversight of RRIC activities, the OSHR created, through numerous other activities, more visibility for DRR grant programs during the year.

Just prior to the beginning of the fiscal year, the OSHR planned and held a media briefing in Rochester, New York, on the liquid protein diet. The briefing explained how researchers had shown that protein diets can cause life-threatening heart irregularities. In clinical trials at a GCRC, serious heart arrhythmias were encountered within 10 days of starting the diet.

The briefing, held at the University of Rochester Medical Center, was attended by science and medical writers, together with radio and TV correspondents. During the briefing, a special conference call network was provided by OSHR to medical writers across the nation.

The Associated Press (AP), United Press International (UPI), Gannett Newspapers, New York Daily News, the New York Times, and other media covered the event with extensive stories. Several radio and television networks carried the story, including the CBS Morning News which sent a reporting team to Rochester.

In another Rochester, the Minnesota home of the Mayo Clinic, the OSHR served as a catalyst for a press conference on the Dynamic Spatial Reconstructor (DSR)--the heart of which is a Biotechnology Resources-supported computer center. The DSR, an advanced x-ray device, allows researchers to view the heart, lungs, and circulation in three-dimensional motion. For this project, the Office helped to prepare the media background materials, helped to arrange on-site details, and was responsible for all national media contacts. Among the news media covering the event were the CBS Network News, New York; the Journal of the American Medical Association (JAMA), Chicago; Minneapolis Tribune; Rochester Post Bulletin; the AP; WTCN-TV, KMSP-TV, KSTP-TV, Minneapolis; KAAL-TV, Austin, Minnesota; KTTC-TV, Rochester; and KROC Radio, KAAL Radio, KWEB Radio, Rochester.

Extensive coverage with credits resulted, including in The Washington Post and syndicate; the New York Daily News; JAMA; The Atlanta Constitution; the Jacksonville Journal; Public Health Reports; U.S. Medicine, plus many other print as well as electronic media outlets. Interest in the story continued for months.

The OSHR staffed a press room at the "First Annual Symposium on Computers in Perinatal Medicine," sponsored by the Perinatal Clinical Research Center of Case Western Reserve University, Cleveland. During the meeting, OSHR set up a press briefing involving caesarian birth rate problems. Based on a large-scale study at the Perinatal Clinical Research Center, Cleveland Metropolitan General Hospital, three obstetricians and gynecologists associated with the Center discussed how a certain number of caesarian deliveries might be avoided. The Cleveland Plain Dealer, the Cleveland Press, UPI, WJKW-TV, WKYC-TV, and WGAR Radio in Cleveland covered the event with additional coverage through a conference call set-up. Articles appeared in the New York Times, U.S. Medicine, Science News, OB-GYN News, and many U.S. publications through UPI syndication.

Based on a cover story in the July Research Resources Reporter, the OSHR held a press conference in conjunction with the University of Michigan Medical Center on the development of a drug pump which could be implanted in liver cancer victims. The research featured the work of the Assistant Program Director of the University of Michigan GCRC. Telephone conference call participants in the press briefing included the AP, Washington Bureau; Reuters - Washington; The Washington Post; the New York Daily News; U.S. News and World Report; JAMA; Bioscience; Medical Tribune; Family Health; the Cleveland Press; American Pharmacy; International Medical Tribune; Gannett News Service; Medical World News; Chicago Sun Times; and National Public Radio. Attending the briefing in person were UPI and UPI Photo; Detroit Associated Press; The Windsor Star; the Detroit Free Press; WNEM-TV; WJLB-TV; WXYZ-TV; WDIV-TV; and WWJ Radio in Detroit. Many national stories resulted which led to numerous phone calls to the Michigan GCRC inquiring about the treatment.

The Detroit press briefing was part of a broad communications plan that the University of Michigan GCRC requested from OSHR. The idea behind the plan was that the Michigan GCRC should increase its visibility and enhance its image among three important target audiences: medical professionals, mainly practicing physicians, throughout the State of Michigan; University of Michigan Medical Center professional and support staff; and the general public throughout the State of Michigan. To reach these three distinct audience groups different approaches and techniques were required. After OSHR negotiated with the Michigan Medical Society, their journal, Michigan Medicine, ran an article by the Program Director about the GCRC. OSHR helped to write the article and did final editing prior to publication. Several other projects between the Michigan Medical Society and the Michigan GCRC are pending as a result of the Office's personal contact with the Society.

In Cincinnati, the Office assisted with a demonstration of CLINFO at the University of Cincinnati Medical Center. The new computerized data management system for clinical investigators' display was attended by half a dozen media reporters. The showing involved a live television relay from the CLINFO Laboratory at the Medical Center's GCRC to a conference room in the Medical Center Administrative Building.

The OSHR originated the idea for a twentieth (20th) anniversary celebration for the GCRC Program. The Office developed a plaque honoring "20 years of exceptional service devoted to the improvement of human health through the NIH-funded General Clinical Research Center." This plaque was presented by the GCRC Branch Chief at celebrations at medical institutions whose clinical research centers were 20-years old.

The Johns Hopkins Center was highlighted at the first event which was part of the renowned Saturday Morning Physicians Rounds. The Johns Hopkins GCRC Program Director presented a description of the Center, followed by several scientific presentations pertaining to current research protocols by scientists who had used the facility. The Saturday Morning Physicians Rounds are a fixture at Johns Hopkins and attracted about 300 health care professionals to the event.

In December, a special Program was held at Washington University Medical Center to mark the 20th anniversary of its GCRC. The highlight of the Program, which drew an overflow audience, was a lecture by the Chairman of the Washington University Department of Medicine and former GCRC Program Director. The event resulted in extensive media coverage in the St. Louis Globe-Democrat and on several local television and radio stations.

In mid-January, another GCRC 20th anniversary event took place at the University of Southern California Medical Center in Los Angeles. A local U.S. Congressman was the main speaker at the luncheon which honored the GCRC. The local Program Director was interviewed on several television and radio shows and the opportunity for several feature stories in the print media was developed by OSHR.

The University of Rochester was the fourth clinical research center to celebrate its anniversary. The editor of The New England Journal of Medicine spoke at the Medical Center event. The Program Director made numerous radio and TV appearances arranged by OSHR, including on WOKR-TV, WHEC-TV, and WROC-TV. The Rochester Democrat and Chronicle and the Rochester Times-Union also featured stories on the event, plus pieces from suburban and Medical Center publications.

In March, Ohio State University marked the 20th anniversary of its Center with a ceremony highlighted by a talk from a local Congressman. The GCRC Branch Chief presented a plaque and gave some remarks. The activity generated favorable exposure throughout the Columbus area.

Another anniversary event was organized late in the spring with the encouragement and help of OSHR. Yale conducted a formal auditorium program and a "birthday party" for former patients at the Children's GCRC. The activity received extensive media coverage throughout Connecticut and within Yale University. All media contacts were either initiated or coordinated by OSHR.

OSHR helped to plan and produce the dedication of the DRR-supported Primate Research Laboratory at the University of South Alabama. The 10,000 square foot Research Laboratory housed a breeding colony of squirrel monkeys. A media "Open House" was conducted by OSHR during the event. The Mobile Press Register ran a full-page story with pictures. The Pensacola News Journal ran a lengthy feature in the "South Alabama" section. For electronic media, OSHR placed the facility's Director on a five-part TV series over "Newswatch" WEAR-TV, Pensacola, and made other placements on WALA-TV and WKRG-TV, plus WABB Radio, Mobile. The Acting Division Director and the Animal Resources Program Chief were interviewed by Mobile electronic media.

An OSHR staffer served on the Planning Committee for the Ninth Annual Minority Biomedical Support Symposium held in Albuquerque in April. For the ninth consecutive year, OSHR managed the press room for the Symposium and handled all media placements on local TV and radio, as well as national publicity and features. The AP and UPI moved three stories over the wires, including a lengthy feature on the MBS Program Director.

The National Newspaper Publishers Association sent out an advance release and a follow-up picture to over 200 subscribers. All materials were provided by OSHR.

The Sheridan Network and the National Black Network carried guests over their national hookups. Albuquerque television, KOB-TV, KGGM-TV, KOAT-TV, and radio--KZIA, KABQ, KOB, KRKE--conducted numerous interviews with students, faculty, and Program participants during the event, all of which were arranged by OSHR.

The OSHR sent out an advance release to each Program Director at MBS schools in the United States. This "hometown" news story was adapted by many schools to tell the local MBS angle, while pointing up the national Symposium.

Early in the fiscal year, an article on the DRR Minority High School Summer Research Apprenticeship Program was written exclusively for the National Newspaper Publishers Association by OSHR. The article, together with photographs, was issued by the Association to over 200 predominately Black-owned newspapers throughout the United States.

In October, the OSHR staff held a conference for the public relations and information staff persons from the seven Regional Primate Research Centers. The meeting, held at the Yerkes Regional Primate Research Center, Atlanta, Georgia, was to acquaint Primate Research Center personnel with the latest in informational techniques and approaches and how these might be applied to the

Centers. In November, the OSHR staff spoke to the Primate Center Directors at the Washington Regional Primate Center, Seattle, in order to acquaint them with the earlier meeting and to improve their awareness of the role of the information person at their Center.

A lengthy two-part article in the Washington Star on "Artificial Intelligence--SUMEX-AIM" in December was initiated by OSHR during the previous summer. A hand-delivered press kit, including a copy of "The Seeds of Artificial Intelligence" and an invitation to the Artificial Intelligence Workshop at Stanford University, was given to the writer. The author accepted OSHR's invitation to attend the Workshop, and interviewed many of the major participants. Upon her return to Washington, she contacted the OSHR office, and arrangements were made for several interviews with the prime NIH contact, a DRR Program official, who was quoted in the lengthy story.

With respect to Division publications, during the first six months of the fiscal year, prior to the onset of the Office of Management and Budget's printing moratorium, the OSHR handled the printing of the following publications: "Do We Care About Research Animals" (reprint); "Division of Research Resources Five-Year Plan"; "General Clinical Research Center Patient Information" (reprint); and "The National Institutes of Health Minority (Extramural) Research and Training Programs" (reprint). All clearance and bulk printing of RRIC publications were also handled through the Office.

In addition, the Office received and processed approximately 55 Freedom of Information requests. Approximately 300 hours of clerical and professional time were spent handling these requests. The Office also handled 114 Privacy Act requests which, for the most part, were for copies of summary statements of grants before the National Advisory Research Resources Council. These requests took approximately 475 hours of clerical and professional time.

Finally, a total of 13,162 publications was distributed through the Office during the year. The Office received 7,553 individual mail requests; 305 individual telephone requests, including Congressional inquiries; and 80 individual walk-in requests.

Animal Resources Program

INTRODUCTION

The overall objective of the Animal Resources Program is to support resource projects that provide, or enable scientists to use effectively, animals in human health related research. Special attention is given to those animal resource activities that are broadly supportive of the missions of the various NIH components. The objectives are accomplished through the Primate Research Center Program and the Laboratory Animal Sciences Program.

PRIMATE RESEARCH CENTERS PROGRAM

The Regional Primate Research Centers Program was initiated by NIH during the period 1961-1965. The original objective was to meet a recognized need for suitable facilities and appropriate research environments where biomedical research employing the nonhuman primate could be best conducted. Seven Regional Primate Research Centers (RPRCs) were constructed, equipped, staffed, and became operational as unique research institutions by 1965. These Centers and their respective locations are: University of Washington RPRC, Seattle, Washington; Oregon RPRC, Beaverton, Oregon; California RPRC, Davis, California; Delta RPRC, Covington, Louisiana; Yerkes RPRC, Atlanta, Georgia; New England RPRC, Southborough, Massachusetts; and Wisconsin RPRC, Madison, Wisconsin. Each Center is affiliated with a host academic institution. The Centers have resources and research environments which are suitable for a broad range of biomedical research. The Animal Resources Program provides core operational support for the Centers through resource grants. Research projects at the Centers are funded largely by NIH categorical Institutes, other Federal agencies, and private foundations through grants and contracts. which are held by core staff and collaborative and/or affiliated scientists. Through their use of nonhuman primate models, these scientists have made numerous important contributions to biomedical research. During the past year, investigations have been carried out in various biomedical areas, including reproductive biology, infectious diseases, behavioral sciences, neurosciences, toxicology, nutritional and metabolic diseases, and environmental health.

Core support in the amount of $17.213 million provided by this Program in fiscal year 1981 enabled the 150 core staff, doctoral-level scientists to conduct research in the Centers. In addition, the resources and services of the Center were made available to 554 affiliated, collaborative, and visiting scientists from various academic institutions. Research training environments were provided for 181 graduate students engaged in thesis related research. The Program provided salary support for 665 doctoral level, technical, and administrative staff personnel.

On a regional basis, the Centers provided a total of 7,700 biological specimens to 351 scientists at various research institutions throughout the United States. Scientific productivity within the seven Centers has remained strong during the past year, with 696 journal articles and books published by the core staff and affiliated/collaborative scientists.

Because of the problems associated with obtaining certain species of nonhuman primates from countries of origin, all seven Centers have continued their domestic breeding efforts. Approximately 2,100 infants and fetuses were produced by the seven Centers in 1980, representing nearly 75 percent of their total primate animal requirements. Nuclear colonies of a number of less commonly used primate species have also been maintaind to assure the survival of these species for potential research needs in the future. A total of approximately 12,000 primate animals representing 45 species were maintained by the Centers in 1980 for research and domestic breeding uses.

Major research emphasis areas and selected examples of research activities at each Center during the past year are as follows:

WASHINGTON REGIONAL PRIMATE RESEARCH CENTER, UNIVERSITY OF WASHINGTON AT SEATTLE

The core research program of the Washington RPRC includes the areas of neurological scientices, cardiovascular function, developmental biology, disease models, endocrinology and metabolism, and craniofacial structure and function. An extensive affiliated scientist program involved over 60 investigators who were engaged in a variety of investigative areas. An example of research activities during the past year is as follows:

Antiplatelet Drugs

During the past year investigators at the Washington Center have continued to screen selected high probability oral agents that modify platelet function in order to determine efficacy and dose regimens. Two to three baboons (*Papio cynocephalus*) are used continuously in this particular project. The results are of substantial interest in the strategy of designing controlled human clinical trials. In a second set of studies, the effect of cardiopulmonary bypass oxygenation on platelet function was evaluated. The results showed that there is a marked transient defect in platelet plug forming capability during cardiopulmonary bypass that is associated with selected platelet alpha granule release. In a follow-up study, it was shown that the infusion of PGI^2 into the oxygenator at an appropriate dose completely blocked the generation of the platelet dysfunction. These data show that the defect in platelet function is secondary to platelet activation by the oxygenator. Eighteen animals were used in these studies. The publications resulting from this work have created a great deal of interest among clinical circles because they provide insight into an important complication of cardiopulmonary bypass surgery. In a third set of experiments, 10 animals were used to evaluate the thrombogenicity of coagulation factor IX concentrates. These concentrates have been shown to be thrombogenic in hemophilia β patients when given in large volumes, as is required for surgical procedures. By measuring the rate of platelet and fibrinogen destruction, as well as the appearance of platelet alpha granule proteins (PF4 and β-thromboglobulin) and thrombin-derived fibrino-peptides from fibrinogen following the infusion of various commercial factor IX concentrates, it has been possible to provide comparative information on the thrombogenicity of these clinically applied preparations. The use of nonhuman primates in these studies has been of particular importance and provides unique information of interest to all hematologists caring for patients with hemophilia β.

OREGON REGIONAL PRIMATE RESEARCH CENTER, OREGON HEALTH SCIENCES UNIVERSITY

Major areas of research emphasis at the Oregon RPRC include reproductive biology, perinatal physiology, cardiovascular pathology, cutaneous biology, immunology, nutrition, toxicology, and metabolic diseases and behavior. An example of activities during the past year is as follows:

Cholesterol Gallstones: Plasma Lipoproteins and Bile Composition

Scientists at the Oregon Center have shown that nutritional, endocrine, and genetic factors influence the concentrations and metabolism of plasma lipoproteins. In addition, there are strong indications that these factors affect the development of atherosclerosis and cholesterol gallstones in humans. The latter diseases were demonstrated in squirrel monkeys (*Saimiri sciureus*), which were fed semipurified diets containing cholesterol and a saturated fat in studies on the relationships between plasma lipoproteins and cholesterol gallstones.

Female Bolivian squirrel monkeys were shown to have a much higher incidence of gallstones and greater concentrations of high-density lipoproteins (HDLs) than male Bolivian squirrel monkeys. Since this is analogus to findings between men and women, Bolivian squirrel monkeys may prove to be a useful model for studies on differences between the incidences of gallstones in men and women.

Comparative studies between both sexes of Brazilian and Bolivian squirrel monkeys revealed that Bolivian squirrel monkeys have more insoluble pigments in the gallbladder bile than Brazilian squirrel monkeys. Concentrations of an unconjugated pigment (bilirubin) are greater in the plasma of Bolivian monkeys than in the plasma of Brazilian monkeys. This increased concentration is associated with reduced rates of clearance from the blood of both bilirubin and sulfobromo-phthalein.

CALIFORNIA PRIMATE RESEARCH CENTER, UNIVERSITY OF CALIFORNIA AT DAVIS

The major reserach areas at the California Center relate to environmental health siences, infectious diseases, perinatal biology, behavioral biology, respiratory physiology, and immunology. An example of activities during 1980 is as follows:

Fetoscopy Techniques for Sampling Fetoplacental Circulation

The goal of this project is to develop procedures which will permit sampling of the fetoplacental circulation in early human pregnancies in order to diagnose inherited genetic diseases, e.g, the fetal hemoglobinopathies. This study has involved the use of pregnant rhesus monkeys and baboons as animal models to advance the technology of fetoscopy and to assess the safety of the procedure for both mother and fetus prior to its use in the human population.

The fetoscopy procedure has been successfully carried out in 19 cases (83 percent of attempted cases) of pregnant baboons between 80 and 100 days gestation. The position of the fetus and the monodiscoid placenta is determined prior to fetoscopy, using noninterventive ultrasonar techniques. The fetoscope is placed directly between the ventral body wall and into the uterus, and an umbilical or placental blood vessel is sampled using a small gauge needle introduced into the fetoscope cannula. After this procedure, pregnant animals are permitted to go to term and compared with a control group to assess any possible perinatal wastage associated with the procedure.

Based primarily on this work with nonhuman primates at the California Center, approval has been granted by DHHS to extend the fetoscopy study to pregnant women who have elected to undergo abortions. The initial application of the procedure in pregnant women is for early detection of inherited anemias; i.e., sickle cell anemia, thalassemia. This progression of events in the development of fetoscopy clearly demonstrates the significance of the nonhuman primate as an animal model in the study of human disorders.

DELTA REGIONAL PRIMATE RESEARCH CENTER, TULANE UNIVERSITY

The Delta RPRC core research programs cover the areas of microbiology and infectious diseases, immunology, parasitology, biochemistry, neurobiology, and urology. The affiliate/collaborative program includes a number of other areas, including vision research. An example of their research projects is as follows:

Leprosy in Mangabeys

A sooty mangabey (_Cercocebus atys_) which had developed a spontaneous case of lepromatous leprosy was received at the Delta Center early in 1980. Biopsy material taken from this animal was used to inoculate two other mangabeys. Both of these inoculated animals have demonstrated clear evidence of leprosy. The organisms recovered from the index case are indistinguishable from human _Mycobacterium leprae_.

This primate model of lepromatous leprosy offers exciting potential for further investigations. The model will permit this disease to be studied in a primate host which has never been possible until now. The index case has now progressed to the point where deformities in the appendages have resulted from nerve damage. If this condition can be reproduced in inoculated mangabeys, it will be possible to study new methods of intervention and experimental corrective surgery. The potential significance of a primate model for studies on this disease is underscored by the fact that over 15 million lepers currently exist in the world.

This project represents a cooperative effort between the Delta RPRC and Yerkes RPRC, with four of the animals currently under study provided from the Yerkes Center colony. In addition, efforts on the immunological aspects of leprosy are underway at both Centers, with active plans for further collaboration in which the Yerkes Center will provide for breeding and reproductive biology studies on sooty mangabeys for this project.

YERKES REGIONAL PRIMATE RESEARCH CENTER, EMORY UNIVERSITY

Research at the Yerkes RPRC includes psychobiology of great apes and monkeys, anatomical and physiology aspects of the central nervous system, muscle pathology, reproductive biology, immunology, and language acquisition. An example of their activities during the past year is as follows:

Long-Term Effects of Radiation Exposure in Rhesus Monkeys

A colony of rhesus monkeys exposed to various types and amounts of radiation has been studied for the past 15 years at the Yerkes Center. The colony includes three types of radiation exposure: 1) atomic bomb detonation at the Nevada test site in 1957; 2) gamma irradiation with cobalt 60 in 1958; and 3) neutron irradiation in 1954. This irreplaceable group of animals has been monitored closely for 25 years and is believed to be the only colony in the world with such a unique radiation exposure history and long-term followup. The colony has shown an extremely high incidence of cancer (48 percent of autopsy cases have had one or more types of cancer), and a majority of these (85 percent) have occurred in radiation-exposed animals. The control animals are comparably aged rhesus monkeys with no radiation exposure. The cancer incidence in exposed animals has increased over time, and even higher incidences of cancer can be anticipated as these animals grow older. The incidence of cancer in which animals have died in various exposure groups includes 58 percent in the atomic bomb exposed group, 75 percent in the neutron radiation exposed group (3 of 4 animals), and 38 percent in the gamma radiation exposed group.

This work will provide important information in regard to the cancer producing potential that may be associated with radiation exposure. Specifically, these studies will provide data relevant to the incidences and types of cancer which occur in a population of aging, radiation-exposed monkeys. The research will also provide information on cancer tissues and cells for a variety of experimental studies as well as data regarding the possible role of cancer viruses in primate tumors. Information will also be available on the long-term cancer producing potential of various types and doses of radiation. These studies should provide data relevant to problems which may occur in exposed human populations.

NEW ENGLAND REGIONAL PRIMATE RESEARCH CENTER, HARVARD UNIVERSITY

The New England Center's core research program covers the areas of microbiology and infectious diseases, psychobiology, comparative pathology, viral oncology, cardiovascular physiology, and nutrition. The Center's extensive affiliate and collaborative research programs include numerous other biomedical areas of investigation. An example of research activities at the Center during the past year is as follows:

Cardiovascular Physiology

The contribution of the renin-angiotensin system and the autonomic nervous system to maintenance of arterial blood pressure was studied in adult *Macaca fascicularis* (cynomolgus) monkeys. The objective of these studies was to measure the hemodynamic characteristics of reversible renin-dependent hypertension using partial constriction of the abdominal aorta and to study the renal and endocrine responses to infusions of agents into a lateral ventricle of the brain. The renin-angiotensin system influences vascular resistance, sympathetic nervous system activity, renal functin, and blood pressure level. The central nervous system influences autonomic function, the renin-angiotensin system, endocrine functin, and salt and water balance. All of these components of the cardiovascular, endocrine, and nervous systems are involved in experimental models for producing and maintaining arterial hypertension.

After experimentally producing acute renin-dependent hypertension in *Macaca fascicularis*, studies with this model revealed a dependency on the renin-angiotensin system and the ability to block any rise in arterial blood pressure by injecting converting enzyme inhibitor (teprotide). Several synthetic peptides that are competitive inhibitors of renin were tested in this model to demonstrate the feasibiity of blocking the actions of renin directly.

Acute hypertension in *M. fascicularis* was also produced by infusions of angiotensin II while measuring renal function, blood pressure, drinking behavior, and endocrine responses. Additional experiments demonstrated the physiological effects of agents administered to animals who became renin-dependent through aortic constriction or following sodium depletion. Future studies will be directed toward determining the contribution of central nervous system function in renin-dependent hypertension.

WISCONSIN REGIONAL PRIMATE RESEARCH CENTER, UNIVERSITY OF WISCONSIN AT MADISON

Focused areas of research at the Wisconsin Center include endocrinology, behavior, neuroscience, reproduction, and pathology of environmental pollutants. An example of research performed during the past year is as follows:

Primary Influence of Central Nervous System on Initiation of Puberty

Although scientists have attempted to determine the mechanism of the onset of puberty ("how does puberty start?") for more than a century, knowledge in this area is still incomplete. Studies with rhesus monkeys (*Macaca mulatta*) at the Wisconsin Center, however, indicate that maturation of the brain (the hypothalmus) which stimulates the release of luteinizing hormone releasing hormone (LHRH) is a key factor for the initiation of puberty. LHRH is known to stimulate the release of pituitary gonadotropin (LH and FSH) which facilitate the secretion of ovarian steroids (estrogen and progesterone), the maturation of the ovarian follicles, and induce ovulation. Before initiation of puberty, the release of gonadotropins (and LHRH) is very small but is drastically increased during the pubertal period. Furthermore, the increase of gonadotropins (and LHRH) during puberty is characterized by the release in a pulsatile rhythm (one pulse every hour), and a diurnal rhythm (more prominent during the night than during the day). Since both pulsatile and diurnal rhythms of hormones are observed in neonatally ovariectomized monkeys when they reach the nominal age for puberty, the ovary is not the organ determining the time of onset of puberty. Similarly, since the pituitary can fully respond to LHRH before puberty, it was concluded that the maturation of the brain is a key factor responsible for the onset of puberty and not the maturation of the pituitary. Although the mechanism of the initiation of the rhythmic and increased release of LHRH is not known, these findings will contribute to understanding the mechanism of puberty and also to establishing a new method for clinical treatment of human patients with delayed puberty.

LABORATORY ANIMAL SCIENCES PROGRAM

The Laboratory Animal Sciences Program (LASP) assists institutions in developing and improving animal resources for biomedical research and training through the award of research and resource grants and contracts. Program areas include support for research related to improving health care and determining environmental requirements of animals used in research; animal colonies of unusual and and special value for research; studies directed at finding animal models which are needed for research on human diseases; projects to assist institutions to comply with the legal and policy requirements for care of laboratory animals; laboratories for the diagnosis and control of diseases of laboratory animals; and research training of specialists in the field of laboratory animal medicine. The Program awarded funds totaling $7.715 million in fiscal year 1981, which supported 60 grants and 6 contracts relevant to animal research or resource projects, 9 institutional training programs, and one individual fellowship award.

RESOURCE RELATED RESEARCH

The majority of projects falling into this category involve investigation of the etiology, pathogenesis, and control of laboratory animal disease problems. For example, currently active projects include the diagnosis and control of mammalian encephalitozoonosis, pathogenesis of parvovirus infection in canines, experimentally induced mucoid enteritis in rabbits, and control of respiratory mycoplasmosis in rodents. The mycoplasmosis project has resulted in development of an enzyme linked immunosorbent assay (ELISA) for detection of anti-*Mycoplasma pulmonis* antibody in mice and rats. Results to date indicate (1) a continued high incidence of mycoplasma infections in both conventional and cesarean derived and barrier maintained colonies, (2) cultural isolation of the organisms in barrier maintained animals appears to be more difficult than conventional animals, which may be due to environmental differences or bacterial synergism, and (3) the absence of infection in isolator maintained animals suggest that ELISA false positives are minimal. Thus, the ELISA test appears to be a sensitive, specific diagnostic test that has many advantages compared to other available diagnostic tests, especially for wide-scale screening.

In addition to disease related studies, several projects involving population studies, classification, and breeding of nonhuman primates are currently active. The population studies include a long-term evaluation of natural rhesus populations in northern India and definition of important habitat features for West African rain forest primates. Extensive field work in Peru, Brazil and Colombia plus study of museum specimens is currently underway as part of a comprehensive project to establish definitive taxonomies of the various cebid monkeys with particular attention to those species of significance to biomedical research; namely, Saimiri (squirrel monkeys) and Aotus (owl monkeys). Present taxonomic classification of these latter species is confusing and incomplete. Better definition is critical to captive propagation and research efforts which may depend on demonstrated linkages between genotype and phenotype. The eventual goal is to publish the information as Volume 2 of Living New World Monkeys (Volume 1 dealt with Callitrichidae, the family that includes marmosets and tamarins).

A relatively new project (initiated in 1979) involves genetic investigations in rhesus monkeys at the Wisconsin Regional Primate Research Center. In particular, additional genetic markers are being sought in order to develop a multiple locus measure of inbreeding. This work is an extension of previous efforts to identify usable polymorphisms in rhesus monkeys for parentage identification. Information from this project will be important in understanding and measuring inbreeding in captive populations, particularly with the limited importation of new animals to augment existing breeding colonies.

The number of resource related projects has been relatively level in recent years (9-12 active projects). There is a growing recognition that naturally occurring laboratory animal diseases and environmental factors can have a significant effect on research projects. In recognition of this need, the support of research projects dealing with important laboratory animal disease problems was selected for emphasis in the recently prepared Five Year Plan.

ANIMAL MODELS AND SPECIAL COLONIES

The major objectives of this program area are: (1) to define, characterize, and exploit the relevant biological attributes of selected animals which display potential for use in several areas of biomedical research and (2) to establish, improve or expand special colonies of well characterized animals which are of proven value for biomedical research, but which are not generally available from other sources. Projects aimed at the first objective are of two general types.

The first is represented by two active resources (Washington State University and Michigan State University) which involve a multidisciplinary effort to identify, characterize, and make available new animal models of human genetic diseases. Input regarding potential models is sought from a variety of sources, including animal clinics, veterinary practitioners, and breeding associations and clubs. The oldest resource of this type is at Washington State University. This group has worked with 30 animal models or potential animal models during the past three years including 7 new ones recognized during this period. Some are now well established and have separate grant support including Ehler-Danlos syndrome of dogs, mink and cats (autosomal dominant disease with defective collagen formation), combined immunodeficiency disorders in horses, and juvenile type diabetes mellitus in dogs. Other models are still in the early stages of development such as mucolipidosis in cats, inherited feline tremors, and inherited canine myasthenia gravis. The general approach is to establish colonies of affected animals and begin characterization studies, often in collaboration with experts at other institutions who are interested in a specific model. Animals and materials from the various models are made available to interested investigators. Ultimately, some models may be transferred to other groups with the interest and expertise to carry on further studies.

Other animal model projects are oriented around selected species which have potential utility as models in more than one categorical area of research. Several marine invertebrate projects, in particular, exemplify this approach. Declining natural populations and problems of maintaining species such as the sea hare, Aplysia californica, sea urchins, Strongytocentrotus purpuratus, and loliginid squids have limited research utilization in the past. Development of mariculture and maintenance techniques could favor laboratory breeding over procurement from the ocean and lead to a continuous source of species wherever they were required. Considerable success has been achieved in maintaining adults of these marine species under laboratory conditions. For example, at the Kerckhoff Marine Laboratory, California Institute of Technology, a culture maintenance system for sea urchins has been developed which can contain up to 3,000 adults. This system provided sea urchin eggs and embryos throughout the year for a laboratory group of 20-30 individuals and during "out of season" periods for other workers. It is now possible to stock and reuse animals for several years. Increasing environmental pressure (chemical pollution, commercial collections for food) gives added impetus to current goals of this resource relative to finding new deep-water populations developing cryogenic methods for storage of fertilized eggs and embryos, and growing sea urchin larvae and carrying them through metamorphosis in the laboratory.

Special colony projects combine in varying degrees the maintenance and production of special strains or stocks of animals with ongoing research to further development and characterization of the models. Currently supported projects include a hamster resource at the University of Texas, Dallas; a bullfrog (Rana catesbeiana) resource at Louisiana State University; a congenic mouse resource at Sloan-Kettering Institute; a rabbit inbred and mutant stock resource at the Jackson Laboratory; and a mouse mutant gene resource also at the Jackson Laboratory. The latter project is typical of this group. The original mouse colony included some 140 mutants with a focus on endocrine, neurological, and immunologic problems. The specific aims are to maintain these well-defined stocks to discover new mutations in the mouse and develop stocks of new and established mouse mutations for use as animal models in biomedical research and to make mutants available to the scientific community. Nearly 3,500 mice were supplied to investigators last year either as breeding stock or experimental animals. A charge is made for this service and the funds are returned to the grant. New mutations kept for further study include an autosomal mutation affecting myelin, a recessive autosomal mutation that affects balance and an inherited hypothyroidism. The mutant gene in the latter model is inherited as an autosomal recessive gene. The thyroid gland in these mice is small and produces almost no T_4 (one of the thyroid hormones). Their symptoms are almost identical to primary hypothyroidism in humans, and future work with this mouse mutation will be aimed at gaining an insight into the cause of human primary hypothyroidism.

Support for projects related to animal model development and the establishment of special animal colonies decreased from the previous year's level; i.e., FY 1980 - $1.912 million (25% of LASP budget) versus FY 1981 - $1.623 million (23% of LASP budget). A total of 15 projects received support, compared with 24 in FY 1980. This reduction was in keeping with the Five Year Plan which provided for decreased emphasis in this area, particularly if funds were reduced for the program. The development and characterization of new models did receive special consideration as evidenced by the one new award in this area, i.e., to develop laboratory culture techniques of Octopus for biomedical research.

INSTITUTIONAL ANIMAL RESOURCE IMPROVEMENTS

Institutional animal resoure improvement projects are awarded to help institutions upgrade their animal facilities and develop centralized programs of animal care in support of their biomedical research programs. A major objective is to enable institutions to comply with the Animal Welfare Act and DHHS policies on the care and treatment of animals. Requests of this type usually include animal cages to meet current regulations, general sanitation equipment such as cage washers, renovations of animal facilities, and addition of trained professional and technical personnel. The projects are supported for one to three years, after which time the applicant institution is expected to take over complete financial responsibility for its basic animal resource.

Institutional improvement projects have been supported since the inception of the Laboratory Animal Sciences Program. Requests of this type peaked in FY 1973 following implementation of the Animal Welfare Act of 1970 (P.L. 91-579) and the DHHS policy on animal welfare. Over the past 10 years, 113 institutions have received improvement grants with awards totaling approximately $15.0 million. The following figures represent the trend during this period:

	FY 74	FY 76	FY 78	FY 80	FY 81
Reviewed	19	19	21	12	16
Approved	12	9	13	8	16
New Awards & Supplements	36*	6	3	4	2
Total Active Projects	46	21	11	6	7
$ Awarded (in $1,000s)	3229	1289	793	783	298
Percentage of Budget	51%	23%	10%	10%	4%

*Includes applications reviewed in FY 73.

The above chart indicates a relative steady rate of new proposals in recent years. The largest number of program inquiries still touch on this area.

The ability to fund new projects of other types and to combat inflationary costs has come largely at the expense of this program area (note steady decrease in number of active projects and $ awarded). It was possible to fund only one new application and one supplement this year.

Data from the National Survey of Laboratory Animal Facilities and Resources (published March 1980; fiscal year 1978 data) revealed the following facts relative to facilities and equipment:

- Approximately 16 percent of all nonprofit biomedical research organizations reported a need for replacement of some animal facility space now in use, 38 percent reported a need for remodeling to protect the integrity of space now in use, and 43 percent reported a current need for additional space.

- Approximately $350 million is required to meet current needs of nonprofit biomedical research organizations for space replacement, remodeling, and additions to their animal facilities. Another $407 million (using FY 1978 estimated construction costs) will be required to meet space needs projected for FY 1988.

- Nonprofit biomedical research organizations reported a current need in their animal facilities of $43 million for equipment renovation, replacement or additions.

The survey indicates in particular a need for biohazard containent space and equipment, which reflects changes in research activities and increased recognition of the need to contain hazardous agents. In order to meet needs of the scale indicated by the survey, legislative authority (new construction and major renovation) and substantial funding over a period of years would be required.

RESOURCE LABORATORIES

The objectives of these laboratories are to provide for improved animal health programs through appropriate surveillance activities and investigation of naturally occurring disease and other laboratory animal problems, to support studies resulting in new information on diseases of laboratory animals and their etiology, to aid in the elucidation of new laboratory animal models of human disease, and to develop resources including tissues, slides, photographs, etc., for research and training. Resource laboratories have been a major program activity for over 10 years. There has been a continuing turnover in the institutions receiving such awards (support has been terminated for 14 laboratories). The total number has remained relatively constant (13-16) in recent years, and approximately 32% of the budget is awarded in this area. Since resources and trained personnel are limited; laboratories have been confined to those settings with at least several million dollars of NIH-supported research involving the use of laboratory animals. Most resource laboratories are institutional in nature; however, in several instances it has been feasible to serve more than one institution in a metropolitan or regional area.

There are 15 programs which are currently being supported. One new laboratory was funded during FY 1981. This laboratory represents a somewhat different emphasis than previous projects, in that it will deal with marine species. Located at the Marine Biological Laboratory at Woods Hole, Massachusetts, the laboratory will operate on a year-round basis to monitor the health of marine animal used in research at Woods Hole. It will be the first major effort to investigate the etiology of infectious and noninfectious diseases of marine fish and shellfish used in biomedical research. Results of the activities proposed should provide much needed information relevant to the culture, health, and maintenance of marine laboratory animals.

Laboratory activities encompass a broad spectrum ranging from surveillance and monitoring to conduct of research on important laboratory animal disease problems. The laboratories have been productive in terms of new information and techniques. A fatal SV 40 (simian virus 40) infection in a young rhesus monkey was recognized by one laboratory. This agent is widespread in monkey populations and was introduced into many people with some of the early polio vaccines. It had never been associated with a rapidly fatal illness in an otherwise healthy animal before. This case was also of significance because it demonstrated the usefulness of the immunoperoxidase technique in finding virus in autopsy tissues. Bacterial pathogens are commonly associated with serious disease outbreaks that interfere with or compromise research.

Avian tuberculosis was diagnosed in a colony of White Carneaux pigeons used in pharmacologic studies at one institution. Intradernal tuberculin testing proved to be unreliable because of the frequent occurrence of false positive and false negative reactions. Birds not being used were culled from the colony. A protocol was developed for effective quarantine of the remaining animals, routine disinfection of equipment and cages, and protection of personnel to reduce the risks of exposure. Using these methods, the organism was successfully contained until critical studies were completed. The colony was subsequently replaced with animals from another source shown to be free of disease by the diagnostic laboratory.

Recognition of a Salmonella typhimurium-associated conjunctivitis in an adult cat during quarantine led to initiation of a Salmonella screening program at one laboratory in the northeast. A Salmonella carrier incidence of slightly over 10% was detected in rural source cats from commercial dealers. A high incidence of antibiotic resistance was noted in treating affected cats. The fact that clinically normal carriers of Salmonella can shed organisms is of importance to biomedical research because the organisms pose a potential health hazard for persons handling these animals and the stress of hospitalization or surgery may induce severe clinical disease.

Several laboratories are particularly interested in the problem of pasteurellosis, a widespread disease of laboratory rabbits. Unfortunately, Pasteurella multocida infections are not readily controlled through antibiotic therapy, and recurrent infections are common. Current studies range from a characterization of virulence determinants and rabbit neutrophil phagocytosis and/or killing to identification of important serotypes to vaccine studies using avirulent mutant strains. Several separate research grants have been submitted dealing with specific aspects of this complex problem area. Information being generated has been valuable in understanding the multifactorial nature of this bacterial pathogen and should lead to the development of improved means of control for this important disease.

Recognition of potential animal models is an important aspect of working up problems presented to the laboratory. One laboratory recently recognized an abnormal susceptibility to viral and bacterial infections in a colony of Brittany spaniels with an inherited degenerative disease of the central nervous system. Clinical and diagnostic workups of these animals showed that a group of animals in this coloy were totally or partially deficient in complement (C-3), a blood factor essential for resistance to injury of all types. Although research has only begun, this deficiency appears to be inherited as a simple recessive trait. It is a very rare condition and these animals are extremely important for their potential use in the study of disease resistance and the inflammatory response, not only in dogs but in all animal species.

OTHER PRIMATE RESOURCES

In addition to the seven Regional Primate Research Centers, the Animal Resources Program supports several other nonhuman primate resources. These include three contracts and five grants for the domestic breeding of nonhuman primates. In addition, there is a grant for a Primate Supply Information Clearinghouse. These projects are part of the effort to provide a supply of primates for essential biomedical research in the face of export restrictions and embargoes by the countries of origin. During fiscal year 1981, no wild-caught rhesus monkeys were imported for biomedical research. The supply of other wild-caught Old World as well as New World primates continued to decline due to increasing export restrictions. The three contracts are for the production of animals for general distribution to NIH extramural investigators. The overall goal of these projects is to produce 1,200 rhesus monkeys and 150 cynomolgus monkeys per year. As of June 30, 1981, there were 1,622 female rhesus and 142 cynomolgus in the production colonies. There were 997 rhesus and 118 cynomolgus monkeys born this past year. The polio vaccine testing program took the first 235 male rhesus offspring. All females were kept for colony expansion. In addition, ARB supplied 344 rhesus monkeys to NIH grantees from cull, exchange, or recycled animals. The contracts also supplied 160 young females to Lederle Laboratories for expansion of their colony and provided 78 cynomolgus monkeys to investigators.

The grant-supported primate breeding projects are for establishing nuclear production colonies and determining proper husbandry techniques for maintaining these colonies. Colonies under development are baboons, two species of marmosets, squirrel monkeys, and two species of Galago (bushbabies). The latter project represents the one new award in this category during the current fiscal year. In addition to these breeding and development grants, the Caribbean Primate Center at the University of Puerto Rico has a grant supporting an island colony of 900 rhesus monkeys. These monkeys have genealogy records dating back to 1938, making them very useful for social and behavior studies. The Center is also conducting some pilot studies on tropical diseases and physiology with primates housed on the mainland. The National Institute of Neurological and Communicative Disorders and Stroke maintains a colony of rhesus at the Center for fetal studies.

The Primate Supply Information Clearinghouse is designed to facilitate maximum research utilization of primates already in this country. The Clearinghouse matches requests for primates, primate tissues, and related services with investigators and breeding colonies who have these items available. The Clearinghouse publishes a weekly bulletin and has handled 735 formal requests for primates and 1,161 informal requests during FY 1981. From these, they placed 3,342 living primates and satisfied 64 requests for cadavers, tissues, and other specimens plus 14 cage requests.

TRAINING

Training in laboratory animal medicine is intended to prepare individuals to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepare to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as a member of a research team.

There are eight currently active training programs with a total of 29 funded trainee positions. In addition to the institutional programs, one individual postdoctoral fellowship was active at the end of the fiscal year. Since the average training period is two and one-half years, there are usually 8-10 graduates per year. Currently available figures indicate that 169 trainees and fellows have completed training since the inception of the training grants and fellowships in laboratory animal science and medicine. Fifty-nine (59) of these are employed by medical schools and 64 by other academic, research or governmental organizations. The majority (104) are serving as directors or staff members of a vivarium; 50 are engaged in teaching and research or are obtaining additional training; and 15 are in public health, private practice or are retired. Retention in the field of laboratory animal medicine has been excellent, emphasizing the career orientation provided by the training and the continuing need and opportunities available for such individuals.

For the past six years, the active training programs and diagnostic resources have been encouraged to employ veterinary students during their summer break. Nine programs and 21 students participated this past year. Critiques of the students involved were submitted to the Branch and, in turn, distributed to all the program directors. It appears that this work experience is resulting in greater knowledge and interest in the field of laboratory animal medicine by veterinary students. Several former summer students entered formal postdoctoral programs this year and development of a "pool" of such individuals for future postdoctoral training should result in long-term benefits to the field.

ADMINISTRATIVE ISSUES

During fiscal year 1981 the effect of earlier proposed legislation to redirect monies scheduled for research using animals to research using technology which might be alternatives to laboratory animals took on a new importance. Interested Congressmen and members of the public were able to pursuade NIH of the importance of this issue and of the need to hold a conference. This resulted in the "Conference on Trends in Bioassay Methodology" held February 18-20, 1981, at the Pan American Health Organization Building, Washington, D.C. This conference produced a record of the advances in technology which might be considered as substitutes for laboratory animals in the pre-clinical phase of research and testing. The state of the art was reviewed by scheduled speakers in an objective way, but the 20 humane society/animal welfare groups who were recognized at this conference were able to build a record favorable to the "alternatives" cause and pursuade many of the senior NIH staff members attending that they represented a signficant political movement. It is expected that this will lead to changes in the way animal research protocols are reviewed, with emphasis on the appropriate use of laboratory animals. It is hoped that Congressional hearings on the alternatives issue can be put in their proper perspective and that the interest in providing for the improvement of laboratory animal facilities and care can be stabilized, if not improved, in the future.

The Animal Resources Program continues to survey the use of laboratory animals in NIH research projects and has obtained data from both the CRISP (computer) system and from personal review of summary statements for FY 1980. These summary statements note the use of laboratory animals in the Description section. Summary data for those study sections in which the most pre-clinical work is done indicate that about 65 percent of these projects use animals, the heaviest use, of course, being of laboratory rodents. This data is similar to that obtained on funded research projects in earlier years. Nevertheless, 13 percent of these research projects continue to use dogs and cats, and well over 5 percent of the projects use primates. There is an increase in the use of farm animals, probably replacing dogs and cats; and there is an increase in the use of marine invertebrate species due to the new opportunities for use because of lower costs and ready availability. The Animal Resources Program will continue to track the use of these animals in the future and is currently considering the funding of more projects in support of amphibian and marine species than it has in recent years.

Table I

Primate Research Centers Program Appliations - FY 1981

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New................	-	--	-	--	-	--
Renewal...........	2	5,649,734	2	5,207,467	2	4,240,744
Supplemental.......	1	2,631,813	1	2,631,813	1	2,666,878
Continuation.......	4	11,928,617	4	10,880,297	4	10,305,303
TOTALS	7	20,210,164	7	18,719,577	7	17,212,925 3/

Table II

Laboratory Animal Science Program Applications - FY 1981

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New................	64	7,241,653	53	4,448,865	6	712,730
Renewal...........	20	2,258,287	20	1,862,469	12	1,502,794
Supplemental......	8	174,166	8	165,666	8	232,690
Continuation......	34	3,834,653	34	2,944,767	34	4,157,396
TOTALS	126	13,508,759	115	9,421,767	60	6,605,610

Table III

Laboratory Animal Science Programs - FY 1981

Program	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
Resource Research..	31	1,758,105	23	1,113,574	12	716,593
Primate Resource...	9	1,390,886	9	1,079,803	5	1,019,278
Special Colonies and Models........	25	2,418,938	24	1,838,599	14	1,566,292
Basic Improvement..	22	3,784,264	22	2,275,711	7	298,190
Diagnostic Labs....	21	3,133,360	21	2,285,339	15	2,275,208
Reference..........	6	676,038	6	554,166	4	634,404
Information & Other	8	200,486	6	131,243	3	95,645
Research Career....	1	37,800	1	37,800	-	--
New Investigator...	3	108,882	3	105,532	-	--
TOTALS	126	13,508,759	115	9,421,767	60	6,605,610

1/ Direct Costs Only

2/ Includes Indirect Costs

3/ Includes Reimbursement Funds ($45,660) from NIA

Table IV

Contract Program - FY 1981

Program	Number Supported	Amount Funded
Special Colonies and Models..........	1	57,043
Primate Supply......................	3	319,952
Program Support.....................	2	125,000
TOTALS	6	501,995

Table V

National Research Service Award Program - Institutional - FY 1981

Type	Number Rec'd	Amount Requested1/	Number Appr	Amount Approved1/	Number Funded	Amount Funded2/
New...............	-	--	-	--	-	--
Renewal...........	-	--	-	--	-	--
Supplemental......	-	--	-	--	-	--
Continuation......	8	700,224	8	748,347	8	574,935
TOTALS	8	700,224	8	748,347	8	574,935

Table VI

National Research Service Award Program - Individual - FY 1981

Type	Number Received	Number Approved	Number Funded	Amount Funded
New................	1	1	1	19,040
Renewal............	-	-	-	--
Supplemental.......	-	-	-	--
Continuation.......	-	-	-	--
TOTALS	1	1	1	19,040

Table VII

Short Term Training Program Applications - FY 1981

Type	Number Rec'd	Amount Requested1/	Number Appr	Amount Approved1/	Number Funded	Amount Funded2/
New................	4	90,450	3	68,340	-	--
Renewal............	-	--	-	--	-	--
Supplemental.......	-	--	-	--	-	--
Continuation.......	1	50,250	1	24,120	1	13,025
TOTALS	5	140,700	4	92,460	1	13,025

1/ Direct Costs Only 2/ Includes Indirect Costs

Fiscal Year 1981 Annual Report
Biotechnology Resources Program
Division of Research Resources

Background and Summary of Past Accomplishments

The Biotechnology Resources Program (BRP) was initiated in 1962 in response to a Congressional interest that NIH establish an activity focused on specialized equipment needed for biomedical research. Since that time, the BRP (formerly called Special Research Resources) has changed and expanded its scope. While the Program in the early years, mainly supported large general purpose computer centers in medical schools, it later moved into an extremely broad and innovative array of biomedically relevant technologies. In addition, the Program now places greater emphasis on regional and national sharing of resources. Major thrusts of the Program today are applications of biomedical engineering, computer science and knowledge systems to biomedical and clinical research programs, and specialized instrumentation for the study of biological structure and function.

Technical capabilities provided by the BRP continue to be essential for progress in many areas of scientific investigation. Without advanced technological resources, biomedical research scientists would be unable to make important structural and chemical measurements or to handle the vast amount of data required to reach valid scientific conclusions.

Over the years, physical and mathematical theories have been developed and subsequently used by engineers in order to provide responsively important research instrumentation necessary for solving problems in biomedical research. That interface between scientists and engineers, so essential for the scientific advancement of biomedical knowledge, is not always obvious nor easily established. Through its operation at this interface, the BRP has been able to develop and make available advanced, highly sophisticated research tools for biomedical science.

BRP has developed and made available to scientists a wide range of computer systems for study of biomedical problems. Among the more recent are computer systems for applying artificial intelligence methods to biomedical problems, computer graphics systems for study of three-dimensional structure of proteins, nucleic acids, interactions of proteins and drugs, and structure of nerve cells and fibers. The development of the first high field 600 Megahertz nuclear magnetic resonance spectrometer for biomedical research was supported by BRP in collaboration with NSF. BRP introduced the first million volt electron microscopes dedicated to biological research in this country and in the world and supports high resolution scanning transmission electron microscopes used in resolving single atoms in cells and tissues. BRP has made the high intensity and tunable wavelength synchrotron radiation available to investigators for studies involving X-ray diffraction, X-ray spectroscopy and time-resolved fluoresence measurements. Access to laser microbeam equipment for subcellular, cellular and tissue level microsurgery is possible for scientists at a Biotechnology Resource.

FY 1981 Accomplishments

Administrative

New Resources - BRP funded two new resources this fiscal year. A high voltage electron microscopy resource was funded at New York State Department of Health in Albany. The grant expands operation of the Albany high voltage electron microscope by providing funds for addition of another shift for use by investigators in the Northeast part of the country. Research will involve three dimensional studies of cancer cell invasion, structure of spindle components during mitosis, cytochemistry and immuno-labeling of thick sections and whole cells, three dimensional reconstruction of cell organelles by tomography, elemental analysis and electron diffraction of wet specimens using an environmental chamber and high resolution dark field study of the structure of membranes. A resource for high sensitivity multinuclei nuclear magnetic resonance spectroscopy and sophisticated data processing was established at Syracuse University, Syracuse, New York. This Resource will develop probes for optimized high sensitivity ^{13}C and other nuclei, implement a new spectral data processing package having unique capabilities for utilization and presentation of raw spectroscopic data, design a hardware/software system to enable users remote to the Resource to have on-line access to the Resource computer and spectrometer and design a data processing center which allows data base searching activity, numerical computation and computer-assisted communication with Resource users.

A new investigator research award was given to Heang Tuy, University of Pennsylvania, to investigate new methods for three-dimensional computer tomography reconstruction from data from a limited range of views and to compare these methods with existing methods on computer simulated and real clinical data.

New Grant Applications

BRP announced the availability of $2 million of new funds for the support of new grants in the May 16, 1980, issue of "NIH Guide for Grants and Contracts," the August 1980 issue of "Federation Proceedings," and the July 1980 issue of the "Research Resources Reporter." Fifteen type one applications and two supplements were submitted for consideration for FY 1981 funding and to date 21 type 1 applications have been received for review at October 1981 and February 1982 Councils. The increase in number of applications received for FY 1982 funding indicates the long lead-time required for writing BRP grant proposals.

Workshops, Conferences and Exhibits

Seven conferences and workshops were sponsored in Fiscal Year 1981. A conference on high voltage electron microscopy (HVEM) in biomedical research was held November 12, 13, 1980, at the University of Pennsylvania, Philadelphia. The conference summarized the important areas where significant advances in the understanding of biological structure and function have been made through use of HVEM, discussed what future developments in HVEM instrumentation would enhance its capabilities, predicted areas of biological research which can be expected to profit from HVEM in the future and evaluated the need for additional HVEM facilities in this country.

A symposium on structure and dynamics in molecular biology was held to celebrate the opening of the Biotechnology Resources Center at the Stanford Synchrotron

Radiation Laboratory October 22, 1980. Speakers at the symposium included Dr. Hans Fravenfelder, University of Illinois, Dr. Steve Harrison, Harvard University and Dr. Michael Koch of the European Molecular Biological Laboratory.

A meeting of Biotechnology Resources Principal Investigators was held May 1, 2, 1981, in Washington, D.C. Topics discussed were fee for service in Biotechnology Resources, BRP annual progress reports, NIH and DHHS patent policies and the research community's concern over support for Biotechnology Resources.

The annual PROPHET Users' Colloquium was held May 14-16, 1981, at Airlie House, Airlie, Virginia. The 125 scientists who attended represented approximately 35 user sites as well as DRR staff including both the BRP and Minority Biomedical Support Programs. Topics discussed included Extended Least Squares Nonlinear Regression, Managing Very Large Data Bases, the Molecular Pharmacology of Digitalis, the Pharmacokinetics and Pharmacodynamics of Cimetidine, Nucleic Acid Sequence Handling Tools in PROPHET, Quantitative Structure Activity Studies, the use of PROPHET in a Major Clinical Center, the Use of Microcomputers with PROPHET, and PROPHET and Distributed Systems. A series of eight workshops was repeated three times to facilitate user choice and attendance. Three special interest groups are developing user recommendations for future directions in the areas of Molecules, Modeling, and Statistics.

A Symposium on Mathematical Modeling of Circadian Systems was held on June 21, 1981, in conjunction with the annual meeting of the Association for the Psychophysiological Study of Sleep in Cape Cod, Massachusetts. The symposium reviewed strengths and weaknesses of various proposed mathematical models of the circadian timing system in predicting periodic biological phenomena.

A workshop on the current state-of-the-art of mathematical modeling in the biological sciences was held July 9-10, 1981, at the Uniformed Services University of the Health Sciences, Bethesda, Maryland. The major computer-based modeling systems in use today were reviewed. The future of mathematical modeling was discussed as well as optimal techniques for the solution of modeling problems. The PROPHET Network was discussed as a potential vehicle for a national modeling resource for biological sciences.

A workshop on technology in support of biomedical research was held at Johns Hopkins University, Baltimore, Maryland, July 30-31, 1981, and August 20-21, 1981. The first session of the workshop defined the problems, obstacles and impediments to application of new technology to biomedical research. The second session examined the various solutions to the defined problems which involved recommendations to NIH on how to enhance and exploit new technology in biomedical research.

BRP showed an exhibit featuring the Resource Directory and Program Guidelines at the Federation of American Societies for Experimental Biology meeting, Atlanta, Georgia, April 13-17, 1981, and at the Fourth Symposium on Computer Applications in Medical Care, November 2-4, 1980, Washington, D.C.

Use of Biotechnology Resources

One of the primary measures of accomplishment that can be applied to BRP is the extent to which its sponsored resources assist the various NIH categorical programs. With their cadres of highly skilled staff scientists and their specialized and often unique facilities, Biotechnology Resources are frequently the scene of productive encounters between experts in a given technology and experts in a given biomedical discipline. Table I gives additional insight into the breadth and depth of this Program on the health research supported by Public Health Service (PHS). Table I lists the number of PHS grants that made use of Biotechnology Resources and awarded dollars to these grants. The distribution of research assisted by the BRP reflects in part how apportionment of research funds to the NIH Institutes and other agencies is made.

The total number of projects conducted in Biotechnology Resources and the number of investigators which made use of Biotechnology Resources are given in Table II for Fiscal Years 1979 and 1980. The number of publications resulting from research projects conducted in Biotechnology Resources in Fiscal Years 1979 and 1980 are also given in Table II.

Research Accomplishments

Biomedical Computing

Computer Processing of Visual Field Data - The visual field is a spatial map of the eye's sensitivity. Examination of the visual field in human subjects plays an integral role in the diagnosis and management of ocular and neurologic diseases. Visual field data, however, represent graphic patterns that must be interpreted qualitatively by trained observers and must be stored in patient records as relatively complex hand-drawn images. The complexity of these graphic images has inhibited their inclusion in automated record-keeping systems. In addition, although the data represent three-dimensional structures, they must necessarily be recorded as two-dimensional images on paper charts.

The Resource at Washington University has designed and constructed a microprocessor controlled recording device that has been interfaced to a standard clinical perimetric instrument. This device is now in use in the Department of Opthamology and allows the recording of the results of all visual field examinations. The recorded examinations are stored locally on small flexible disks which may themselves be included in the patient's physical charts. In addition, the data are also transmitted to a larger visual-field database system contained within a minicomputer system in the Department of Opthamology.

The assembled visual-field database may be used to retrieve patient records for immediate examination and may also be searched cross-sectionally for statistical analyses. Such a capability greatly enhances our ability to assess therapeutic interventions designed to forestall vision loss. Graphic image generation takes place at cathode ray tube display terminals as well as through a hard-copy plotting device. The three-dimensional nature of the data can now be exploited through the use of display algorithms that project three-dimensional surfaces as two-dimensional images using perspective and superposition of image elements to produce the desired visual effect. This process, in turn, promises to produce a truly fundamental advance in the technique of visual field examinations, allowing a more detailed study of specific forms of visual field defects and thereby improving our understanding of pathophysiological events which lead to blindness. The development of this perimetric system has been the result of a close collaboration between the Department of Opthamology and the Biomedical Computer Laboratory.

TABLE I
PHS Support for Investigators Using Biotechnology Resources for FY 1980

NIH Institutes	Number of Grants	Awarded Dollars in $1,000
Aging	6	724
Allergy and Infectious Diseases	44	4,130
Diabetes, Digestive Diseases and Kidney	149	15,066
Cancer	171	19,127
Child Health and Human Development	42	4,418
Dental Research	7	472
Environmental Health Sciences	17	3,337
Eye	43	3,799
General Medical Sciences	299	32,592
Heart, Lung and Blood	127	21,084
National Library of Medicine	7	1,171
Neurological and Communicative Disorders and Stroke	52	4,918
Fogarty International Center	5	106
Division of Research Resources	22	3,924
Total NIH	991	114,867
Other PHS Components		
Alcohol, Drug Abuse and Mental Health Administration	36	3,158
Health Resources Administration	4	461
Center for Disease Control	1	128
Food and Drug Administration	1	24
Office of Health Research, Statistics and Technology	4	423
Total PHS	1,036	119,038

TABLE II

	FY 1979	FY 1980
Number of Projects	1,421	1,346
Number of Investigators	2,088	2,180
Number of Publications		
Papers	863	829
Books	87	76
Abstracts	232	241
Total	1,182	1,146

Computer Graphic Studies of Anti-Cancer Drugs - In collaboration with Dr. Corwin Hansch (Pomona College) the Resource at the University of California, San Francisco, has explored one of the most powerful classes of anti-cancer drugs, those which inhibit an enzyme which produces precursors to DNA. The enzyme is dihydrofolate reductase and a typical drug is methotrexate, effectively used for some years in cancer chemotherapy. Dr. Hansch has studied this system for some time in attempts to design more potent drugs with less toxic side effects. He began studying the three-dimensional structure of the enzyme but found that the molecular models available were too clumsy and inaccurate for the precise fits between drugs and receptor that he needed to study. Beginning in the spring of 1980, he and his postdoctoral associates have collaborated with the Computer Graphics Laboratory in studies of the binding of series of related compounds. This in turn is leading to new syntheses and eventually to new drugs for possible use in the treatment of cancer.

The Formation of Specific Connections among Nerve Cells - It is generally believed that for the brain to function in a correct manner nerve cells must be connected to each other in a very accurate manner. This means that during the development of the brain, each nerve cell must be able to find the correct ones with which to form such connections. In order to find out how a cell does this, and what factors can affect its ability to achieve its normal goal, it is important to determine what events occur during development. For example, does a cell always make the appropriate contacts at first, or is there a period of trial and error, of searching around, until the right targets are found? Furthermore, will a cell form other connections if its normal targets are missing, and with whom? And lastly, to what degree are the connections specified by the genes of the organism, and how are they modified by environmental factors like chemicals, temperature, radiation and so on?

Although in the long run the Resource at Columbia University is interested in the development of connections in the human brain, much simpler nervous systems are studied because they are more accessible to a complete understanding of their structure, function and development. Thus, a very small invertebrate is being studied and then only part of its brain. This part contains a few hundred cells, which have been mapped in detail, both in the adult and at various embryonic stages using the CARTOS computer imaging system. This group of nerve cells is understood rather well, and models have been proposed for the development of its particular connections. In recent work it has been shown, using a microbeam to destroy or alter certain cells instruct others as to their fate, and trigger their development. Thus, it has been shown that the problem of development is not "simply" one of autonomous cells finding other particular autonomous cells to connect to, but that the cells themselves are defined by who they contact. It is expected, therefore, that factors that affect the interaction of cells in development would lead to the formation not only of abnormal connections, but also to the making of unusual or abnormal cells.

GENET - An Experiment in Artificial Intelligence (AI) System Dissemination - The MOLGEN project at Stanford has focused on applications of artificial intelligence and symbolic computation to the field of molecular biology. The research began in 1975 and is currently in the first year of a three-year grant renewal. In early 1980 it was realized that some of the systems developed by MOLGEN were of direct utility to many scientists. Accordingly, with the cooperation of the SUMEX-AIM staff and close coordination with the AIM Executive Committee, it was decided in February 1980 to provide a carefully limited guest service for the community use of such systems. Two programs, SEQ and MAP, were made available to the national academic community. SEQ is a general purpose nucleic acid sequence analysis system and MAP is a program which determines restriction sites from enzymatic digest data. Investigators have free dial-up access from almost anywhere in the United States to these capabilities. Over 300 researchers at over 80 institutions have used this service. There were two major reasons for the establishment of this guest service, which took the form of the GENET account on SUMEX. The first was to broaden MOLGEN's base of scientist collaborators, to find molecular biologists at institutions other than Stanford who could contribute actively to our knowledge-based approach to problem solving. The second was to introduce a generally computer-naive community to the benefits of resource sharing provided by a system like SUMEX, with the hope of serving as a model for the dissemination of other AI software and possibly for an eventual resource for molecular biology.

GENET has been important both for MOLGEN and for the national community (over 200 users) of molecular biology. It has ensured a steady flow of ideas for the artificial intelligence research that is core to both the MOLGEN grant and the SUMEX-AIM mission. It has also provided a useful service to an international community that is not readily available elsewhere.

The University of Washington/Northwest Consortium - Substantial progress toward an industry-university consortium supporting the design of very large scale integrated (VLSI) circuitry, the next wave of the burgeoning microelectronic industry, has been made recently. Each of several industrial members of the consortium will advance $50,000 start-up funding and commit to yearly dues contributions. The biomedical research computing of our collaborators will certainly benefit from the application of VLSI technology. This University of Washington Resource will draw upon its substantial experience with biomedical laboratory automation to apply VLSI advances.

This activity brings closer a date when we can be developing VLSI systems for medical uses. The start-up costs for VLSI work are far beyond the monies that NIH can expect to expend. This Resource is trying to utilize industrial and Defense Advanced Research Projects Agency funds to accomplish the start-up without asking for direct funding from NIH. When it is ready for production of specific biomedically justified projects, it will submit grant requests via the usual channels to support this activity. This may occur as early as next year.

Biomedical Engineering

Potassium Sensor - The Biomedical Electronics Resource at Case Western Reserve has undertaken a potassium sensor collaborative project with Abbott Laboratories in Chicago. Abbott Laboratories provides a biochemist, a mechanical packaging engineer and an electronics engineer for final advanced development who work directly with the Resource staff. The proposed sensor is hand-held and disposable. Abbott will provide the evaluation data, packaging and will construct the instrumentation. IC Engineering of Arizona will fabricate the sensor's electronics. The Resource will do the feasibility studies and supply the technological know-how.

Biological Structure and Function

Nanosecond Spectroscopy - The facility of the Center for Fast Kinetics Research (CFKR), University of Texas, is being used by an investigator from the University of Texas to map label sites in ribosomes. The technique utilizes the fact that pairs of photo-activated molecules having the proper characteristics can interchange energy across space. The effectiveness of this energy transfer depends on the distance between fluorescent probe species. The CFKR Resource can provide precise measurements of fluorescence lifetimes in the region of one nanosecond and have been used to obtain measurements between probes attached to the S1 protein of the small ribosomal subunit and to the 3'-end of 16S RNA. Experiments with probes attached to several other locations are in progress.

Spin Label-Oxygen Methods - Scientists at the Biomedical Electron Spin Resonance (ESR) Spectroscopy Center, Medical College of Wisconsin, have developed a new method for measuring oxygen concentration in biological systems using nitroxide radical spin labels as molecular probes. The interactions of oxygen and nitroxide radical spin label cause changes in the ESR characteristics of the spin label that permit determination of the biomolecular collision rate between the two. This rate depends upon the product of the oxygen concentration and the oxygen diffusion constant. The rate of change of the biomolecular collision rate when nitrogen rather than air is suddenly flowed over the sample cell depends on the concentration of oxygen in the sample cell, independent of the diffusion constant. This method is being applied to measurement of oxygen concentrations in liposomes. Other related spin label-oxygen methodologies are being developed.

High Frequency Nuclear Magnetic Resonance (NMR) - Regular scheduling on the 500 MHz NMR spectrometer at the National NMR Facility for Biomolecular Research, Massachusetts Institute of Technology, began in October. The instrument includes a variable temperature probe, high precision temperature control and a sensitive deuterium lock channel. The spectrometer, because of its ease of use and the extensive repetoire of pulse experiments which can be performed, has found great favor with users. Initial studies have included a project on proton nuclear Overhauser effects and protein dynamics in lysozyme, a study of carbohydrates using two-dimensional NMR experiments, and several projects on solution conformations of macromolecules.

The Action of Lithium on the Nervous System - Lithium is an effective treatment for many patients with manic depressive illness, reducing the extremes of mood which characterize that disorder. It is also reported to be effective in the treatment of certain somatic illnesses, for example, hyperthyroidism and granulocytopenia. In addition, a wide range of psychiatric and non-psychiatric nervous conditions, from impulsive aggressiveness to movement disorders, have responded in varying degrees to lithium treatment. There is concern over all of these therapies, since chronic treatment with lithium may cause kidney damage. In none of these therapies is it clear how lithium is exerting its effects, or whether the effects are related. In spite of that, many physiological and biochemical actions of lithium are known, even though their basic relationship to disease and therapy is still unclear. The mechanism of action of lithium is being investigated in the mass spectrometry resource at Washington University, St. Louis, Missouri, and the toxicity aspects of the drug are being studied at the mass spectrometry resource at Rockefeller University in New York.

A major effect of lithium on inositol metabolism in the cerebral cortex has been investigated by Dr. William Sherman in the Psychiatry department at Washington University. Inositol is a vitamin-like substance, since body requirements are sometimes met by diet, although at other times it is made in the body from glucose. In the nervous system, some of the inositol is found as a structural part of certain specialized fatty substances called lipids. These lipids, the phosphoinositides, undergo increased breakdown and synthesis during the transmission of nerve impulses, thus appear to have a role in the function of the nervous system.

Several years ago Dr. James Allison and Dr. Sherman found that lithium treatment causes inositol levels to decrease in the cerebral cortex of rats. The decrease is remarkable, a 30% loss at high doses. More recently, it was found that a metabolite of the phosphoinositides, an inositol phosphate, increases several-fold in concentration while the free inositol is decreasing. This suggestion that lithium interferes with phosphoinositide function is strengthened by another finding, that lithium blocks the activity of the enzyme which converts inositol phosphate to free inositol. Thus, lithium may change the normal levels of these metabolites in tissues, thereby modifying nerve impulse transmission. Whether this hypothesis is true is under active study. It provides some hope that we can obtain insight into the way lithium acts in manic-depressive illness and other disorders.

Lithium has two naturally occurring isotopes, ^{6}Li and ^{7}Li. Human and animal studies indicate that the distribution and toxic effects of Li are isotope specific. Lithium toxicity appears to be due to ^{6}Li but it is not known which isotope is responsible for the therapeutic effects of lithium. Dr. Frank Field of the Rockefeller University is collaborating with Dr. P.E. Stokes of Cornell Medical Center and Dr. F. Brink of Rockefeller University to develop a mass spectrometric method to assay lithium in cells and fluids from manic depressive and control patients.

Both of these studies could lead to a better understanding of the therapeutic and toxic effects of lithium in manic depressive patients. They could also lead to individualized lithium treatment regimens for different patients and indicate ways of avoiding lithium toxicity.

Fiscal Year 1981
Annual Report
General Clinical Research Centers Program Branch
Division of Research Resources

Program Description

During the past year the General Clinical Research Centers (GCRC) Program celebrated its 20th Anniversary. The continued scientific productivity of the Program has amply demonstrated the wisdom of Congress, which in 1959 directed the NIH to establish clinical research centers throughout the country to improve and intensify the scientific attack on human diseases and their basic biologic parameters. As a part of the 20th anniversary celebration, Centers throughout the nation have sponsored seminars by leading clinical scientists and hosted a series of special events for their congressional representatives and the public. This spring, the Director of NIH gave special recognition to the success of the Centers in an address to the national clinical research societies.

Advances and accomplishments in the biomedical sciences have been quite remarkable in the past 20 years, and are documented in various NIH publications. During the past year, the GCRC program, as part of its 20th anniversary activities, has undertaken to document the role of the program in these advances. The initial effort by the Centers has produced a bibliography of more than 6,500 key scientific articles, classified by scientific area. Four areas, including the neurosciences, diabetes, hypertension, and neonatology, have been selected for special reports. Committees have been established in each area to review and document the role of the program in contributing to advances in these important areas of public health.

The CLINFO program has been expanded to several new sites, including Scripps Clinic, Columbia University, and the University of Iowa. These data management resources continue to enjoy a favorable reception from the clinical research community. Individual CLINFO sites have begun to enhance research activities through sharing of information and programs.

The Clinical Associate Physician (CAP) Program has received increasing recognition from NIH as a means of meeting a critical need to attract physicians to careers in clinical investigation. Of former CAPS, more than 90% have entered academic medicine and 50% of these have already successfully competed for NIH grants or contracts.

Typical Center and Program Changes

The typical Center in Fiscal Year 1981 contained 8 beds, staffed by twenty full-time personnel, at a cost of $839,000 (Table I). The program appropriation has grown from $35 million in Fiscal Year 1970 to

$60.148 million in Fiscal Year 1981 (Table II). Although appropriations have not kept pace with the costs of operating the Centers, and the number of beds has decreased, the use of the Centers for research outpatient visits has steadily increased. The productivity, as measured by numbers of publications and abstracts, has shown steady growth over this period.

Table I

ESTIMATED TYPICAL CENTER
(75 Centers)

Funded Fiscal Year 1981

8 Beds

PERSONNEL	FTE	AMOUNT (thousands)
Professional	1.1	$ 65
Administrative	1.4	24
Laboratory	2.4	45
Dietary	3.1	47
Nursing	11.7	216
Other 1/	.9	22
Fringe Benefits (19.5%)		82
	20.6	$501
HOSPITALIZATION		
Routine/Per Diem/Scatter Bed		$246
770 B Patient Days X $105		(81)
327 C Patient Days X $105		(35)
1469 A Patient Days X $60 (Ancillaries)		88
1165 Outpatient Visits X $22 (Ancillaries)		26
		$244
TRAVEL		1
SUPPLIES, EQUIPMENT, OTHER		37
TOTAL DIRECT COST		$783
INDIRECT COST (7% of the Total Direct Costs)		56
TOTAL		$839

1/ Includes 37.62 FTE Clinical Associate Physicians positions.

TABLE II

GCRC PROGRAM, 1969 - 1981

FY	CENTERS	POSITIONS FTE	FUNDED BEDS	PATIENT DAYS A & B & C	OUTPATIENT VISITS	APPORTIONMENT (in thousands)
69	93	2,298	1,023	245,943	---	$ 35,004
70	93	2,076	904	244,824	1,175	35,004
71	82	1,885	881	234,870	14,515	38,004
72	84	1,867	907	238,152	23,654	42,181
73	83	1,790	893	227,501	36,280	41,300
74	87	1,795	877	232,534	50,614	42,320
75	84	1,732	823	223,269	50,020	42,619
76	84	1,727	784	222,488	56,217	42,533
77	82	1,679	755	204,369	65,130	47,283
78	79	1,706	633	193,151	71,049	51,946
79	74	1,622	613	198,000	86,215	51,941
80	75	1,694	602	195,880	101,216	56,720
81	75	1,547	593	186,958 (est.)	87,395 (est.)	60,148

HIGHLIGHTS OF THE GCRC PROGRAM FY 1981

PATHOGENESIS

Paget's Disease

Paget's disease of bone is a common, painful disorder of aging. Drugs and surgery are used as treatments, but curative therapy can only be developed when the cause of the disease is discovered. Efforts in this direction have been stimulated recently by the finding of virus-like structures in certain bone cells of patients with Paget's disease. Evidence has been obtained for the presence of a respiratory syncitial virus or some related agent in these cells. If the virus can be isolated and used to produce bone disease in an experimental animal, thus proving the virus to be the cause of the disease, the findings could serve as the basis for a new approach to the treatment and prevention of this significant public health problem.

Uremia

Patients with chronic kidney failure have abnormalities in the functions of the nervous, musculoskeletal, blood forming, and reproductive systems. These derangements have for generations been thought to be due to a toxin or toxins in the blood of patients, but these have never been identified. During the last few years evidence has accumulated that parathyroid hormone is one major uremic toxin. Since the state of excessive parathyroid hormone concentrations can be prevented or treated, this finding opens the way to treatments which could ameliorate the uremic syndrome.

Prostatism

Enlargement of the prostate, which obstructs the outflow of urine and can cause infection and kidney damage, is a nearly universal change in aging men. It is known that testoterone from the testes must be present for prostate enlargement to develop. Recent work provides a basis for understanding this important disorder. Aging men show an impaired ability to metabolize dihydrotestosterone (DHT), formed in the body from testosterone. DHT is a growth hormone for the prostate. This work not only provides an understanding of the pathogenesis of prostate enlargement, but suggests possible new therapies based upon control of the enzymes which control synthesis and degradation of DHT.

Hypoglycemia

A series of studies, some involving collaboration between several CRCs, has demonstrated that the hormone glucagon plays a primary role in recovery from hypoglycemia (low blood sugar), that epinephrine largely compensates for deficient glucagon secretion, and that recovery from hypoglycemia does not occur in the absence of both glucagon and ephinephrine. Patients with insulin-dependent diabetes mellitus (IDDM) have blunted glucagon responses, and are dependent on ephinephrine action for recovery from hypoglycemia. There are important practical implications to these findings, as antagonists to some of the actions of epinephrine are commopnly prescribed for disorders, such as hypertension and agina. If given to patients with IDDM, these agents could put these patients at risk for serious hypoglycemia.

Alzheimer's Disease

Recent evidence suggests a familial occurrence of Alzheimer's disease, a mental deterioration beginning in middle life. Moreover, an excess frequency of Down's syndrome (mongolism) has been found among the relatives of patients with Alzheimer's disease. These observations support the hypothesis that Down's syndrome and Alzheimer's disease have related genetic defects, and suggest that Down's syndrome should be considered as a prenatal diagnosis in pregnant women with a family history of Alzheimer's disease.

Alport's Syndrome

New data indicate that at least 1% of renal failure in males in the Rocky Mountain region of the United States is accounted for by hereditary nephritis ("Alport's Syndrome"). A biochemical marker, "hereditary nephritis protein", has been found in the urine of these patients, and seems to be identical with C3bi, part of the complement system involved in fighting infection. This and other evidence suggest that hereditary nephritis may be a defect of complement metabolism.

Photosensitivity

A circulating photoreactive factor has been found in some patients who are very susceptible to the ultraviolet component of sunlight, developing hives and wheals after exposure. Current studies are attempting to identify this factor.

Diabetes

Some new information has been obtained about the occurrence and management of complications in children with diabetes mellitus. A high percentage of newly diagnosed diabetic children have significant alterations in the electroencephalogram, and in some of these the alterations persist for as long as a year. Also, 60% of adolescents with diabetes for more than six years have signs of minimal retinopathy. Too-rapid correction of metabolic abnormalities in teenagers with longstanding diabetes under poor control may precipitate rapid deterioration in the eye condition.

PREVENTION

Hyperthermia

Certain patients develop musculoskeletal rigidity and very high body temperature (malignant hyperthermia) when exposed to some anesthetic agents. Two groups of susceptible individuals, belonging to families in which the condition seems to be inherited, have been identified on the basis of metabolic responses of muscle biopsy specimens. These studies open the possibility of developing a screening test which could predict the risk of malignant hyperthermia, preventing this possibly lethal complication of routine anesthesia.

Renal Stones

Pregnancy results in the transfer of large amounts of calcium from mother to fetus. Maternal calcium supplementation is widely practiced. In recent years, it has been recognized that maternal calcium absorption in the GI tract increases in pregnancy, and that this is due to placental production of 1,25 dihydroxy-vitamin D. Now the first prospective systematic study of mineral metabolism has shown that urinary calcium excretion and 1,25 vitamin D levels are markedly elevated in pregnant subjects. This is analogous to the common renal stone-forming state (absorption hypercalciuria) and suggests that calcium supplementation in pregnancy is unnecessary and probably dangerous.

DIAGNOSIS

Breath Tests

Analysis of the breath has been attracting increased interest as a non-invasive, accurate method of diagnosing systemic diseases. The recently-developed xylose breath test, for example, has a 92-95% reproducibility in the diagnosis of malabsorption, compared to 35-38% for bacterial culture of the intestine, previously the best method. The breath test also does not have the high false-negative rate or the demanding technical requirements of the culture method. A breath test has also been used to identify cirrhosis in narcotic addicts who are being maintained on methadone. This is important because methadone metabolism may be significantly altered in patients with liver disease.

Deafness

An automated system has been developed to measure changes in body movement following an auditory stimulus, for use in detecting hearing loss in neonates. This non-invasive, portable device has a small false-positive error and a negligible false-negative error.

Black Lung Disease

A relatively simple, non-invasive diagnostic test, total respiratory resistance mesured by the forced oscillation technique, can be used as an indicator of early stages of soft coal miners' pneumoconiosis.

Short Stature

A recently developed assay system allows the reponsiveness of patients to growth hormone to be measured by a test of their blood cells in culture. With this test it was demonstrated tha the rare form of short stature known as Laron dwarfism is due to a lack of tissue responsiveness, rather than to a deficiency of the hormone. This is the first such clinical application of a tissue culture assay known, and it opens up the opportunity of determining the hormonal responsiveness of a patient without the need to actually inject hormone and do complex physiologic studies. Follow-up studies indicate that the responsiveness of tissues to insulin can also be assayed by the tissue culture method.

THERAPY

Hypercalcemia

Hypercalcemia (elevatd blood calcium) is a common complication of certain malignancies, especially multiple myeloma and metastatic breast and lung cancer. It causes great morbidity and significant mortality. In a series of 12 patients with this disorder, it was found that a new drug called dichloromethylene diphosphonate (Cl_2MDP), which inhibits bone resorption but not mineralization of new bone, returned serum calcium to normal levels in 11 of them. There was no evidence of significant toxicity. This study suggests that Cl_2MDP may be of major value in the management of this serious clinical problem.

Iron Toxicity

Long-term transfusion therapy is commonly used for anemias of chronic disease, such as the hereditary anemias. This therapy is effective, but leads to a cumulative, toxic body burden of iron, which has been assumed to be significant only after many years. However, recent studies have demonstrated damage to heart, lungs, and endocrine glands after even short-term therapy (months). This is important because it means that therapy with the subcutaneous infusion of desferrioxamine, a drug which can bind iron and remove it from the body, should begin early.

Heart Irregularities

Although certain kinds of arrhythmias are benign in normal children, they often presage sudden death in children with abnormal hearts. The usefulness of phenytoin in the treatment of ventricular dysrhythmias in children has been demonstrated by successful treatment in 95% of those with abnormal heart conditions. A new dosage regimen has been developed which reduces the length of time required for effectiveness from one week to two days.

Tourette's Syndrome

Basic studies in this Clinical Research Center have indicated that Tourette's syndrome, a disability of mental development, is much more common than previous thought. An elucidation of the steps in its neurochemical pathology has led to a new medical approach. Clonidine, a centrally acting drug which affects norepinephrine metabolism, has been shown to ameliorate symptoms of Tourette's syndrome in many patients who were previously unresponsive or unable to tolerate the standard medical approach, haloperidol.

Failure of Maturation

The open-loop pump developed for the continuous subcutaneous infusion of insulin into diabetics is proving to be of use in other disorders as well. For example, the pulsatile delivery of growth hormone is effective in the treatment of hypogonadotropic hypogonadism, a pituitary disorder which prevents normal adolescent maturation. Long-term studies of nocturnal pump-delivered pulses of hormone are now underway in this disorder.

Cancer Treatment

A totally implantable drug delivery system for regional cancer chemotherapy is being used with striking success. The system delivers high concentrations of cancer-fighting drugs directly to the tumor site without causing the degree of systemic toxicity and side effects typical of conventional chemotherapy techniques. The response rate for hepatic tumors, for example, has been 85%, four to five times the rate with conventional chemotherapy. Continuous drug delivery to the tumor area is achieved by a small infusion pump secured in a pouch just under the skin. For treatment of liver cancer, a small catheter leads from the pump directly into the hepatic artery.

Chronic Pain

Unlike acute pain, which warns of tissue damage, chronic pain serves little useful biological function. It can cause sufferers to seek repeated surgery and to risk narcotic addiction in search of relief. Now electrostimulation of the brain by a pocket-sized device enables certain pain victims, some of whom were previously invalided by their pain, to lead lives free of pain and drug dependency. The FDA-approved device stimulates the periqueductal region of the gray matter of the brain, causing it to release beta-endorphin, a normal brain compound with pain-masking effects.

Short Stature

Until recently it was thought that only growth hormone-deficient children could benefit from growth hormone (GH) treatment. It is now known, however, that injections of GH can increase the stature of some short children with normal levels of GH. Together with the recent production of GH by recombinant DNA technology, this finding opens exploration of clinical possibilities such as treatment of short stature accompanying juvenile rheumatoid arthritis, Turner's syndrome, and other disorders, as well as more rapid repair of wounds, bones, and cartilage.

Trauma

A series of GCRC studies has led to significant practical contributions to decreasing the morbidity and mortality in severe trauma, the leading cause of death in young people. For example, the administration of ethacrynic acid to reduce swelling of cerebral gray matter reduces the mortality rate and improves the functional level in patients with severe isolated closed head injury. Also, it has been shown that the common practice of using drugs to paralyze patients who are being mechanically ventilated with positive end-expiratory pressure if they make inspiratory efforts reducing airway pressure, is not necessary or even desirable. In a similar way, it has been shown that patients who require respiratory support should not be removed from end-expiratory pressure to breathing through an endotracheal tube at ambient end-expiratory pressure (T-tube test). The data suggest that endotracheal intubation should be accompanied by low levels of continuous positive airway pressure, and patients should be extubated directly from there. Another example is the demonstration that injured patients who require endotracheal tubes do better if they receive continuous positive airway pressure (if they are breathing spontaneously) or positive end-expiratory pressure (if they are not).

Hypertension

Captopril, an angiotensin converting enzyme inhibitor, is an effective drug for the treatment of hypertension, but it has recently been found to have a high incidence of side effects and a high rate of hypersensitivity. A new, chemically-similar angiotensin converting enzyme inhibitor, MK-421, has been found in preliminary studies to be equally effective, and to have a higher potency and longer duration of action, permitting use of much smaller doses and causing many fewer side effects.

Hyperlipidemia

Recent studies have led to a liberalization of dietary recommendations for patients with hyperlipidemia. Shellfish, previously eliminated from diets for these patients because of the high cholesterol content, may be consumed in amounts of up to three ounces per day without affecting the cholesterol level. Moreover, the consumption of up to six to eight ounces of fish per day may have a significant lipid-lowering effect. These findings have practical importance in adding to the palatability of diets for hyperlipidemia.

Renal Osteodystrophy

Renal osteodystrophy, characterized by failure to grow, bone pain, bone deformities, and frequent fractures, is the most important complication of chronic kidney failure in children. Conventional vitamin D therapy is often unsuccessful and frequently causes hypercalcemia (toxic elevation of blood calcium). The osteodystrophy has now been found to be a heterogeneous disorder, occurring in several forms; to develop even in patients with only mild or moderate chronic renal failure, at a time when their clinical examinations, blood studies, and x-rays are normal; and to respond in most ways to the administration of the vitamin D metabolite 25-hydroxyvitamin D_3, with a negligible incidence of hypercalcemia.

Infertility

The drug clomiphene and intranasal luteinizing hormone-releasing hormone (LHRH) were used to induce ovulation in eight chronically anovulatory patients who were under treatment for infertility. All had failed to ovulate in response to clomiphene even when the drug was given in combination with human chorionic gonadotropin in therapy. Clomiphene, 100 mg. per day, was given on days five through nine of the menstrual cycle and synthetic LHRH was administered intranasally from day 11 to day 14 to induce late follicular development and ovulation. Five of the eight patients ovulated and three of these conceived. Combination therapy with clomiphene and intranasal LHRH offers a new means to treat anovulatory infertility.

Obesity

Two studies have indicated undesirable side effects of the low calorie, high-protein carbohydrate-free diet. Endurance was markedly reduced, muscle glycogen was not spared, and visceral proteins were reduced in subjects on this diet as compared to those ingesting a small amount of carbohydrate. In the markedly obese diabetic on a low calorie diet, nitrogen retention is significantly better if the diet contains carbohydrate. On the other hand, exercise capability is not impaired on a carbohydrate-free diet of normal caloric content.

Red Cell Aplasia

The human bone marrow disease, pure red cell aplasia, has been found to be of immunologic origin. Many patients with this disorder have an antibody that inhibits blood formation and is toxic to developing red blood cells. This finding has led to a rational therapy, administration of the immunosuppressive drugs prednisone and cytoxan.

About 60% of patients with red cell aplasia respond to this regimen with a remission of their disease and a discontinuance of the need for red cell transfusions. Most recently, it has been shown that children with transient erythroblastopenia, a disease which resembles pure red cell aplasia, also have an antibody that inhibits red cell development.

Chronic Asthma

Patients with chronic asthma are generally treated first with theophylline, cromolyn, and bronchodilators. A few patients, whose symptoms are not adequately controlled with these medications, require continuous use of corticosteroids to relieve chronic debilitating symptoms and to decrease the frequency of recurrent hospitalizations and emergency room visits. The value of maintaining the initial drug therapy in steroid-dependent asthma has been questioned, but recent work has shown that continuing bronchodilator therapy with theophylline when giving steroids increases the number of symptom-free days, decreases the need for other drugs, markedly lowers the amount of supplemental steroids needed, and improves pulmonary function and exercise tolerance. The results prove that maintenance bronchodilator therapy with theophylline can provide clinically important benefits for patients with steroid-dependent asthma.

Laryngeal Papillomatosis

Papillomatosis is a potentially life-threatening proliferative disease of the larnyx, thought to have a viral etiology. Repeated surgery may be required. The synthetic drug polyinosinic, polycytidilic acid stabilized with polylysine (poly ICLC), an inducer of the antiviral agent interferon, has been tried in three patients with this disorder. A five-fold decrease in the frequency with which surgery was required ensued. These results strongly suggest that additional studies of antiviral agents in papillomatous diseases may be rewarding.

Immune Deficiency Diseases

A safe and effective immune globulin preparation is needed for intravenous use. A preparation of modified (reduced and alkylated) immune globulin has been found to be safer, much less productive of side effects, and overwhelmingly preferred by patients, when it is formulated in 10% maltose. This simple change in the formulation of antibody will allow the rapid infusion of large doses of immune globulin, thus improving the management of patients with antibody-deficiency diseases.

Medical Advances

The GCRC Advisory Committee and staff have initiated a review of the role of the Centers in the medical advances of the last twenty years.

As a first step, the Committee and GCRC Program Directors listed some of the important advances in medicine since 1960, and divided them into 32 categories and 254 subcategories. The Program Director of each Center was asked to list its most significant publications in these subcategories. To date, a bibliography of more than 6500 related articles has been compiled. Four major categories were selected by the GCRC Committee for the initial studies: neuroscience, diabetes, hypertension, and neonatology (including immunology). A draft paper on the neuroscience has been presented to the Director, NIH for review. A paper on GCRC contributions to advances in diabetes has been drafted and is currently undergoing editing. Plans have been made for committee to sudy hypertension and neonatolgy during the coming year. When the project is completed, the role of the GCRC program's progress in many areas of great importance to public health will be clearly documented.

CLINFO

During the past fiscal year, six production versions of the CLINFO System were installed (University of Cincinnati, Yale University, Mayo Foundation, Peter Bent Brigham Hospital, University of Minnesota, Scripps Clinic). The CLINFO System, a computer-based data management system, was specifically developed for the clinical investigator. Testing of three prototype systems at Baylor University, University of Washington and Vanderbilt University was completed by June 1977, and the results revealed that the system was acceptable to the clinical investigator and that it would be a useful data-management tool. Bolt, Beranek and Neuman, Inc. (BBN) was competitively selected to be the commercial purveyor. The first production systems were installed at Duke University and Johns Hopkins University in late 1978.

Each of the production versions of the CLINFO System, except one, has been heavily used, averaging an estimated 5215 connect hours per week. The CLINFO software can now be used unaltered on several Digital Equipment Company (DEC) computers, thus allowing use of a smaller, less expensive two-terminal version of the System; a grant for one smaller system has been awarded and will be evaluated. Enhancements continue to be made in the software, an important one being that the maximum number of patients per study has been increased from 300 to 5000, which should accommodate all but the largest clinical trials. The position of System Managers under the direction of the CRC was proven critical to the succsss of the CLINFO project.

The second annual meeting of the CLINFO System Managers took place in April 1981. There was more participation at this meeting by the System Managers who manage the production version. The occasion provided a valuable opportunity for them to exchange experiences and ideas with each other and with representatives of BBN and NIH. The meeting was highlighted by the establishment of a CLINFO System Managers Organization and selection of its Charter Committee. In addition to an annual meeting, the System Managers can also communicate their ideas and problems through the CLINFO Newsletter.

Installation of each new CLINFO System has gone smoothly. This has been helped by Dr. Howard Thompson, who is an experienced CLINFO user and Clinical Professor and who is under contract to the GCRC Branch to assist investigators and the System Managers with installation of a new CLINFO System. The purveyor, BBN, has also been successful in responding to problems providing excellent maintenance of the production versions, and improving the software by issuing new versions which incorporate user suggestions.

The future of CLINFO will be determined by periodic meetings of CLINFO Advisors reporting through the CRC Advisory Committee. Such a group was convened recently to advise the GCRC Program on the future course of CLINFO and related data management problems. It made several recommendations: 1. The GCRC Program should examine very closely the suitability of Centers for CLINFO, particularly making certain that control and direction of the CLINFO System reside with the Center and the users. 2. The System Manager should continue to be an integral component of the system. 3. In order to have better estimates of CLINFO usage, a transaction log program be added to the software. 4. The System Managers should design a plan to document the need for advanced statistical capabilities. 5. The BIOINFO proposal of the Biotechnology Program to produce software that will make it possible to run CLINFO on a variety of computer hardware should be encouraged. 6. The group and the Program should further explore the usefulness of PROPHET as a data management resource.

Clinical Trials

The Contract: "Evaluation of the Role of Clinical Research Centers in Clinical Trials with Emphasis on Information Processing" was awarded to the Rand Corporation on September 30, 1978. The goals of this contract were to develop a broad understanding of clinical trials, their organizational, administrative, operational, and information processing problems, and potential solutions; and to develop a detailed understanding of the role of the GCRC Program in clinical trials and to recommend methods to facilitate trials which make use of the resource it supports.

The contractor visited carefully selected leaders and experts involved in the process of clinical trials, appropriate people from the staffs of clinical trials coordinating centers, leading clinical investigators from cooperating clinics and personnel at GCRCs involved in the performance of clinical trials.

The contractor found that the GCRCs surveyed had an average of 15 active clinical trials, and that half of the resources were used to support these trials. The typical interviewed director believed that clinical trials create problems in terms of ethics, resource allocations, and funding. Most directors believed that trials could be improved if there would be more outpatient facilities and improved computational resources. Several directors saw a need for more laboratory technicians, social workers, and data collectors.

In their final report the contractor made the following recommendations:

> Provide research data coordinators to support clinical trials.
>
> Make biomedical scientists (e.g., biostatisticians and computer programmer/analyst) available in the GCRCs on a regular but limited basis.
>
> Make the CLINFO data management and analysis system available to clinical trials that use GCRC resources.
>
> Augment the functional capabilities of the CLINFO system to include analysis of covariance, improved data editing, document tracking, sample size determination and randomization.
>
> Provide a computerized nutrition data base and diet calculation program for GCRC dietitians.
>
> Provide fiscal management and word processing computer programs for GCRC administrative coordinators.
>
> Explore methods to improve the quality of clinical trials by helping investigators to improve their practice of research methodology, statistics, and information processing.

These recommendations will be reviewed by the GCRC Advisory Committee this year. While resource limitations may prevent the implementation of many of these recommendations at this time, diffusion of CLINFO data management is proceeding as a high priority program goal.

A final report of the findings and recommendations has been printed by the contractor and has been distributed by the contractor to all GCRCs participating in this study and to all members of the 'Ad Hoc Advisory Committee of this contract. The GCRC Branch announced the publication of this report to all GCRC program directors who did not participate in the study (35) and all of these requested copies of the report. Copies of the report have been requested by a number of individuals inside and outside the NIH.

Clinical Associate Physician Program

A Clinical Associate Physician (CAP) is a young academic scholar, trained in patient care and research through the fellowship level or its equivalent, who is supported by GCRC investigation by working on a GCRC. By supplementing the professional level care of Center patients, providing Core Laboratory assistance, or performing supervisory or instructional duties, the CAP functions as an institutional resource while developing into an independent investigator.

The CAP program has been a successful one, and has attracted a large number of highly qualified applicants. To maintain the competitiveness of the program, the salary of a CAP has been increased from $25,000 to $30,000 (plus fringe benefits), and awards have included $5,000 per year for small equipment, supplies, computer time, and travel. Each grantee institution is to be permitted a maximum of two CAPs (three if there are separate Adult and Pediatric Centers). Budget constraints, however, have required that the GCRC Program no longer accede to requests for a third year of support for CAPs. The plan is to support as many meritorious candidates for two years as funds will allow.

The GCRC Program is currently supporting 46 CAPS, compared with 34 last year, and the number who have completed the program has increased from 42 to 55. Of these 55, 49 have obtained academic positions and 6 are in private practice. The typical "graduate" of the program spends 49% of time in clinical research, 15% in basic research, 27% of time in teaching, and 9% of time in practice. Although the program is relatively new (24% of those who have completed the program did so in the past year), 50% of the "graduates" in academic life have obtained NIH grant support.

The total cost of the CAP program in 1981 was $1.851 million.

Twentieth Anniversary of the General Clinical Research Centers

During this Fiscal Year, the General Clinical Research Centers (GCRCs) Program has been celebrating its 20th Anniversary with many activities across the country.

Most of the 12 charter GCRCs have been involved in a variety of special events ranging from endowed scientific lectures to reunions of former patients to public open houses.

Clinical Research Centers which have participated in 20th anniversary activities to date are located at the following academic medical centers: Washington University, St. Louis; University of Washington; Johns Hopkins University; Yale University; University of Pennsylvania; Duke University; Emory University; University of Rochester; Ohio State University; Vanderbilt University; and the University of Southern California.

A recent report to the Senate Appropriations Committee called GCRC's "a truly unique conduit for the transfer of information and technology from the laboratory bench to the bedside." The report concluded that this "invaluable and irreplaceable national scientific resource... (should) be significantly strengthened."

Last April, Dr. Donald Fredrickson, in one of his last public statements as NIH Director, spoke to delegates attending the clinical research meetings in San Francisco. He told participants: "The clinical research centers are of very special importance. It's quite important to examine what they support--nearly 4,000 research investigators (working) on over 3,000 projects that are supported by the categorical institutes to the tune of nearly $270 million in NIH grants.

"It is around these Centers that we're all going to have to unite...to determine whether or not there are other savings in categorical funds that can be realized by maximizing the use of both (the) inpatient and outpatient facilities in clinical research centers."

Biomedical Research Support Program
Division of Research Resources

Annual Report
Fiscal Year 1981
October 1, 1980 - September 30, 1981

Biomedical Research Support Grant Objective:

To strengthen and enhance the research environment of institutions heavily engaged in health-related research through the use of flexible funds and local decision making which enable them to more efficiently and effectively conduct their biomedical research programs.

This basic objective of the Biomedical Research Support Grant (BRSG), as established by legislative history and intent, is to extend opportunity and responsibility to the scientific/administrative leadership at the institutional level for making specific on-site allocations for biomedical research purposes. This is to assure that a portion of the total NIH funds for biomedical research utilizes local decision making, allowing for appropriate internal balancing of needs as well as early recognition and development of emergent research concepts, techniques and talent.

Program Activities:

- REVISION OF THE REPORTING REQUIREMENTS FOR GRANTEES

In keeping with the Administration's commitment to reduce the reporting burden on academic and scientific institutions the format for the BRSG Annual Progress Report was revised for the reporting period April 1, 1980 through March 31, 1981. A number of specific criticisms and suggestions conveyed to us by the grantee community during the previous reporting period were considered in making the revisions. For example, five tables of program specific data were formerly required. In the revised format, only two tables of information on program specific activities are required. Instructions for preparation of the report have been made clearer and adjusted to reflect the deletion of three tables. Information requested in the narrative description section has also been reduced. It is no longer necessary to describe all major research accomplishments during the reporting period. Rather, the institutions are encouraged to describe only one or two outstanding examples of research activities supported with BRSG funds.

Grantee institution response to date has been favorable regarding changes in the format and the reduced reporting burden. Staff analyses of 1981 progress reports now underway will seek to identify other appropriate adjustments for the future.

In Fiscal Year 1980, information supplied by BRSG awardees in their annual progress reports was captured by the DRR Scientific Classification System. It was used in over 25 different reports requested by Congress and other Federal agencies regarding DRR support for a wide variety of scientific activities including heart, lung and blood research, toxicology research, population research, prevention research, and vision research.

- REVISION OF THE BRSG COMPUTATION FORMULA

The following formula was used from 1976 to 1981 to determine the amount of the BRSG made to eligible institutions:

15% of 1st $500,000 of "allowable" research grants base
plus
10% of $500,000 to $2 million
plus
5% of $2 million to $6 million
plus
0% above $6 million

The formula applied to fixed increments of research grants activity the "allowable research grants base), had a cap at $6 million, and a 6:1 "pay out" advantage to the "smaller" institutions as measured by their level of PHS research grants activity (see Table below).

COMPARISON OF BRSG COMPUTATION FORMULA "PAY OUTS"

Type of Institutions	Formula "Pay Out" (cents award/100 cents eligible grants)		
	----------Current Formula--------		Revised Formula Based on
	The 1976 Awards	The 1981 Awards	The 1981 Awards
With least NIH research activity	9.2¢	6.3¢	4.88¢
With most NIH research activity	1.5¢	0.5¢	0.76¢
"Pay Out" Advantage	6.3:1	12.5:1	6.4:1

Since 1976 there has been a disproportional decline in size of BRSG awards to institutions most actively engaged in biomedical research. The static 1976 formula did not adjust for increases in the dollar volume of grants and the number of eligible institutions. In 1981, $596 million of the total research grants base exceeded the $6 million cap; a three-fold increase over 1976. Thus 33% of the total research grants base was not used in the computation of the 1981 awards. This caused an unintentional shift in the distribution of BRSG funds, and had the greatest impact on institutions most actively engaged in biomedical research, since the "pay out" advantage for the "smaller" institutions increased from 6:1 to 12:1.

A revised formula was developed in 1981 in concert with DRR program advisory groups which will be implemented in a 2-step fashion with the first change occurring with Fiscal Year 1982 awards (start date April 1, 1982) and the final step with Fiscal Year 1983 awards (start date April 1, 1983). The new formula removes the $6 million cap; has self-adjusting features to compensate for changes in dollar volume of eligible grants and number of grantees; and returns to the 1976 "pay out" level of 6:1 for the "smaller" institutions.

Using this two-step procedure the BRSG computation formulae for FY 1982 and 1983 will be as follows:

FY 1982 FORMULA COMPUTATION

I 15% of 1st $500,000 of research grants base = $__________
plus
II 10% of $500,000 to $2 million = $__________
plus
III 6% of $2 million to $6 million = $__________
plus
IV 0.6% above $6 million = $__________

TOTAL AWARD = Sum of increments I through IV x Proration Factor[1]

[1] Proration factor =

$$\frac{\text{Total Dollars Available for the BRSG Program}}{\text{Total Dollars Computed by Formula for All BRSG Institutions}}$$

FY 1983 FORMULA COMPUTATION

I 15% of .222 x annual base factor[2] = $__________
plus
II 10% of Increment I to .886 x annual base factor = $__________
plus
III 6% of Increment II to 2.658 x annual base factor = $__________
plus
IV .6% of All dollars exceeding Increment III = $__________

TOTAL AWARD = Sum of Increments I through IV x Proration Factor[3]

[2] Annual base factor =

$$\frac{\text{Research Grants Base (Total "Allowable" Dollars) for all BRSG Institutions}}{\text{Total Number of Eligible Institutions}}$$

[3] Proration factor =

$$\frac{\text{Total Dollars Available for the BRSG Program}}{\text{Total Dollars Computed by Formula for All BRSG Institutions}}$$

Using 1981 data as an example only, the approximate dollar ranges for the Increments I through IV for the FY 1983 formula would be as follows:

Increment	I	0	to	$750,000
	II	750,001	to	$3,000,000
	III	3,000,001	to	$9,000,000
	IV	9,000,001	to	35,000,000

These increment ranges are only shown as examples based on 1981 data and will not be those used in FY 1983.

The impact of these changes in the BRSG computation formula, on the size of awards made to various types of grantee institutions, using 1981 data as a guide, and assuming no change in the BRSG appropriation level and number of eligible institutions would be as follows:

Revised Formula Impact On:

Dollar Increases and Decreases of Award Sizes by Types of Institutions
(as applied to 1981 data)

Types of Institutions	Decreases		Increases	
	No.	Dollar Range	No.	Dollar Range
Medical Colleges	74	$3,123 to $16,109	45	$4,277 to $99,789
Other Health Prof.	89	$12 to $15,264	1	$46,306
Other Academic	150	$2,902 to $17,201	17	$1,506 to $74,270
Hospitals	57	$3,457 to $16,637	5	$41,068 to $63,014
Res. Organizations	82	$3,046 to $16,040	5	$6,870 to $65,135

Shift in Distribution of Funds as Percentage of Total BRSG Appropriation
(as applied to 1981 data)

Types of Institutions	Current Formula % Appro.	Revised Formula % Appro.	Difference % Appro.
Medical Colleges	36.0	40.2	+ 4.2
Other Health Prof.	10.4	9.1	- 1.3
Other Academic	30.1	28.7	- 1.4
Hospitals	10.3	9.9	- 0.4
Res. Organizations	12.8	11.9	- 0.9

- INITIATION OF THE BIOMEDICAL RESEARCH SUPPORT SHARED INSTRUMENTATION GRANT PROGRAM.

Planning discussions and budget projections initiated several years ago culminated in January 1981 with the inclusion of $3.7 million in the Administration's FY 1982 budget request to the Congress in January 1981 for the initiation of a competitive biomedical shared instrumentation program.

The program is being established in recognition of the long-standing need in the biomedical research community to cope with rapid technological advances in instrumentation and the rapid rate of obsolescence of existing equipment. The objective of the program is to make available, to institutions with a high concentration of NIH extramural research awards, research instruments which can only be justified on a shared use basis and for which meritorious research projects are described.

The Program was announced in the NIH Guide for Grants and Contracts, Vol. 10, No. 8, June 26, 1981. The deadline for receipt of applications was October 15, 1981. Applications will be reviewed by specially convened initial review groups of the Division of Research Grants in January and February 1982. Final program advisory will be conducted by the National Research Resources Advisory Council in June, 1982, with awards to be made in July 1982.

Eligibility:

in FY 1982, limited to the 527 institutions which received a BRS grant award in FY 1981.

only one application for a single instrument can be submitted by an eligible institution per annual review cycle.

in contrast to NIGMS Shared Instrumentation Program (meant primarily for NIGMS grantees), the BRS program is intended for a broader community of NIH supported investigators.

Awards:

for direct costs of acquisition of new, or updating of existing instruments.

limited to instruments that cost, at least, $75,000. No upper limit but maximum award is $250,000. Provisions for co-funding.

maintenance, support personnel and service costs are not allowable.

predict funding a minimum of 14 and maximum of 49 awards in 1982.

Conditions:

it is expected that the BRS Program Director and the extant BRS advisory apparatus, augmented with members with appropriate technical and scientific expertise, will be responsible for developing an application, arranging for financing, for placing and for maintaining instrument in operational order and for taking full responsibility for establishing sharing arrangements and monitoring the maintenance and usage of the instrument.

major user group of three or more NIH supported investigators who will use equipment at least 75 percent of the total usage.

minor user group may use the instrument up to 25 percent of the total, these users need not be NIH grantees but priority should be given to NIH supported scientists or to users engaged in health-related biomedical research.

- INITIATION OF AN EVALUATION OF THE BIOMEDICAL RESEARCH SUPPORT GRANT

In December 1980, the General Accounting Office issued a letter report to the Assistant Secretary of Health, Department of Health and Human Services which stated in part --

> "During our survey of the National Institutes of Health's (NIH's) Biomedical Research Support Grant (BRSG) Program, we noted that NIH did not have measurable objectives or a methodology for evaluating the program's effectiveness." and "...the BRSG objectives, as currently established, appear too general to permit NIH to effectively measure the extent to which they are met."

In addition, the Department of Health and Human Services now requires an annual submission of an evaluation plan from each of its constituent agencies.

Thus, the combined force of the GAO and Department's activities has led to a determination that another evaluation of the BRSG Program will be necessary. The last such evaluation was the 1968-1969 Roth-Boyton Report, "The General Research Support Grant Program: Its Objectives and How They are Being Met." The Division of Research Resources has submitted to the NIH a five phase evaluation plan for the Biomedical Research Support Grant Program for FY 1981 and FY 1982.

Phase One - Develop agreed-upon objectives and indicators

Phase Two - Prepare program performance summaries

Phase Three - Prepare design options for full-scale long-term evaluation

Phase Four - Prepare a full-scale evaluation design plan

Phase Five - Implementation

- INITIATION OF A STUDY OF THE BRSG ELIGIBILITY THRESHOLD AND ALLOWABLE TYPES OF GRANTS WHICH MAKE UP THE RESEARCH GRANTS BASE

The eligibility criteria for an institution to receive a BRSG of having at least three allowable PHS research grants totaling $200,000 were established in 1976. In the ensuing five year period the cost of research has increased, the total research grants base "allowable" grants used to compute the size of BRSG award has increased, and the funds appropriated for the BRSG Program have remained stable. The combined effects of these changes have been to reduce the size of BRSG awards to all BRSG grantees, and to raise serious questions about the need to revise BRSG eligibility criteria in relationship to the following issues:

1. Does meeting the current eligibility threshold imply the same level of engagement in health-related research by the grantee institutions as it did in 1976?

2. What is the minimum BRSG award which has a meaningful impact upon the research needs of BRS grantees?

Background:

In 1976, $42.8 million was awarded for the BRSG Program, and in 1981 $44.6 million was awarded; a current dollar increase of 4.2% and a constant dollar decrease of 31%.

In the period of 1976 - 1981:

The number of institutions eligible for BRS grants has grown from 441 to 527, an increase of 19.5%.

The total Research Grant Base (RGB) of BRS grantees had grown from $995 million to $1,785 million, an increase of 79%.

The average institutions' RGB has grown from $2.3 million to $3.4 million, an increase of 48%.

The average R01 has grown from $58,000 to $92,000, an increase of 58%.

The minimum BRSG award has decreased from $17,418 to $12,668, a current dollar decrease of 27%, and constant dollar decrease of 52%.

The mean BRSG award has decreased from $96,954 to $84,584, a current dollar decrease of 13%, and a constant dollar decrease of 42%.

The maximum BRSG award has decreased from $261,305 to $178,699, a current dollar decrease of 32%, and a constant dollar decrease of 55%.

In 1981:

To match growth in average R01 the BRSG award size parameters would now be: minimum $27,520, mean $153,187, maximum $412,862.

Adjustment of the BRSG eligibility threshold to match other changes would result in a FY 1981 threshold of between $300,000 and $450,000.

To match the increase in the average institution's research grants base, the threshold would have to be $300,000.

To match the increase in the average R01, the threshold would have to be $316,000.

To produce a $25,000 minimum BRSG award, the threshold would have to be $400,000.

To meet former NIH Director Shannon's 1968 recommendation to the Assistant Secretary of Health, DHEW (0.025% of total NIH research project to maintain status quo with level of engagement in biomedical research), the threshold would have to be $437,000.

By 1983:

To match growth in average R01 (1983 estimate $105,331, based on 1981 + 7% 1982 + 7% 1983) the BRSG award size parameters would have to be: minimum $31,561, mean $175,680, maximum $473,484.

Adjustment of the BRSG eligibility threshold to match other possible changes would result in an FY 1983 threshold of between $362,000 and $615,000.

To match the increase in the average R01, the threshold would have to be $362,000.

To produce a $30,000 minimum BRSG award, the threshold would have to be $615,000.

To meet former NIH Director Shannon's 1968 recommendation to the Assistant of Health, DHEW (0.025% of total NIH research projects), the threshold would have to be $522,000.

To meet a level of five times the average R01 (an implied value in the Shannon report), the threshold would have to be $525,000.

Allowable Types of Grants Which Make Up the Research Grants Base:

Currently 21 types of research grants are used to determine the research grants base of eligible institutions. Some of those grant types (e.g. P01's, P50's, and P60's) may have resource components similar to those supported by BRSG. In addition, ADAMHA research grants, which are PHS but not NIH support, are allowable toward eligibility. As a part of an examination of the eligibility issue, the question of allowable grant types warrants analysis.

The BRSG program staff intends to focus upon the problems of an appropriate eligibility threshold and types of research grants which make up the BRS Research Grants Base. An analysis of these issues will be conducted and presented to the BRS Subcommittee, General Research Support Review Committee, and the National Advisory Research Resources Council for consideration, prior to making recommmendations to the Director, NIH.

It is anticipated that such considerations and recommendations would be completed in time for implementing any changes by the time of Fiscal Year 1983 BRSG award, i.e. April 1, 1983.

- BRSG BUDGETARY POLICY ISSUE

The current national debate within and between the Executive and Congressional Branches of the Federal Government regarding budgetary policy as it relates to allocation and redistribution of funds among the many public constituencies has raised at least two major general issues. These are the level of funding for programs and the locus of responsibility for their execution (Federal vs local decision making). With an assumption that stark economic reality will dictate a no growth or slow growth policy for many programs of the National Institutes of Health, the question arises within the context of future NIH appropriations as to --

> What should be an appropriate balance for NIH extramural funding between categorical grants and general research support for the mid-1980's?

The Biomedical Research Support Program provides flexible funds which allow the institutions to interpret their most pressing health-related research needs at any given time and to act at the most opportune time and in the most effective way to meet those needs, using funds which are immediately available at the institution. Decisions are made by an advisory group of scientists and administrators working with the institutional program director. BRS assures that a portion of the total NIH support for biomedical research benefits from local insight into institutional research needs and early recognition of emergent research concepts, techniques and talent. The program was authorized by Congress in 1960 to permit the establishment of "grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research..." The balance allowed for by the Congress in the 1960 legislation between categorical funding and flexible funding was a ratio of 85:15 respectively.

This ratio was approximately 92:8 in FY 1969, was approximately 97:3 by 1976, and by FY 1981 the BRSG portion of the ratio was below 2%. Clearly what constitutes an appropriate balance in types of support in an overall no growth situation raises issues that call for active and open dialogue among the populations of individuals and institutions that make up the NIH extramural community.

We have attempted to stimulate such discussions by meeting and corresponding with representatives of a number of national organizations such as the American Association of Medical Schools, Federation of American Societies for Experimental Biology, National Association of State Universities and Land Grant Colleges, American Chemical Society and the Association of Independent Research Institutes.

Readers of this Annual Report are urged to offer their views on the questions to their constituent academic and scientific society so Federal public policy makers can better sense the opinions of this public.

- BASIC DATA TABLES -- AN UPDATE

Table I

Distribution of BRSG Awards by Size

Size of BRSG Award (in thousands)	Number of Grantee Institutions		
	FY 1976	FY 1980	FY 1981
Under $30.0	74	103	101
30 - 49.9	87	89	112
50 - 99.9	116	101	115
100 - 149.9	60	102	88
150 - 199.9	48	106	111
200 - 249.9	19	--	--
250 - 299.9	37	--	--
	441	506	527

Grant Range	FY 1976	FY 1980	FY 1981
Minimum	$17,418	$13,449	$12,668
Maximum	261,305	189,787	178,699
Mean	96,955	88,271	84,584

Table II

Distribution of BRSG Awards by Type of Institution*

Type of Institution	FY 1976	FY 1980	FY 1981
Medicine	106	117	119
Dentistry	26	30	29
Osteopathy	1	1	1
Pub. Health	12	15	14
Pharmacy	13	20	27
Veterinary Medicine	10	9	12
Nursing	3	3	5
Optometry	0	2	2
Hospitals	63	61	62
Health Departments	2	2	2
Research Institutions	71	85	87
Other Academic	134	161	167
TOTAL	441	506	527

* Academic institutions exclusive of health professional school components.

- ILLUSTRATIVE USES OF BRSG FUNDS

1) Pilot Research: Pilot studies test the validity of new ideas and the feasibility of research methods to be used in a particular study, without requiring a large support staff or a lot of materials. This reduces the risk of major cost commitments to projects that might be unproductive and, at the same time, encourages the innovative research that is the bedrock of basic science.

At a mid-western medical school BRSG funds were used to initiate a study on chronically injured livers. Portal vein perfusate flow, portal pressure, and liver weight in the isolated rat liver were monitored in the uninjured and chronically injured states. Preliminary results show that the preparation being used to perfuse the liver is viable, and further studies are testing the feasibility of perfusing both the portal venous and hepatic arterial systems with perfusate containing red blood cells, which may stabilize the chronically injured preparation and allow additional studies on the chronically injured liver. The BRS-funded pilot studies have enabled the scientists to apply for and receive a five-year Clinical Investigator award from the National Heart, Lung and Blood Institutes as well as a one-year grant from the local Heart Foundation.

2) Support of New Investigators: New investigators bring new ideas and new skills that increase the quality and productivity of research. BRSG funding allows them to set up laboratories, conduct initial research and gain post-training research experience until they have established themselves as independent investigators.

At a west coast hospital a young investigator was well trained in both genetics and ophthalmology and was able to use BRSG funds to help launch his research career in academic opthalmology related specifically to children. He has now been able to transplant human cancer tumor in mice, test a new type of cancer treatment, and has undertaken a large scale study on blood samples. The BRSG award helped establish his laboratory and to compete successfully for an NIH grant. He presented his data to an international meeting and was appointed Research Fellow at the Hospital, demonstrating the local, national and international results from the initial BRSG funding.

3) Central Shared Equipment and Facilities: Several investigators may need the same instrument for their individual projects, but could not justify the entire need from any individual grant. Shared equipment minimizes the research costs by avoiding duplication and may reduce the time required to complete certain phases of a project. Overall quality of research may be enhanced through use of shared equipment to answer important questions that otherwise could not have been investigated, or it may improve the precision and reliability of findings.

BRSG funds were also used to strengthen the centrally supported amino analysis facility at a southern university because of the crucial need for amino acid analysis research service by many investigators. The model purchased reduces analysis time to a quarter of that required by the obsolete instrument and also drastically reduces the amount of reagents used. It is expected through establishing a reasonable user fee it will become a self-supporting facility.

4) Provides Interim Funding: Continuity is important to save research projects from being interrupted or abandoned before completion. Interim funding may become critical when a project's continuation grant is approved but will not receive funding for several months. This can force professional and technical personnel into other activities, making them unavailable when project funding resumes. BRSG funding at this point keeps the staff on the project and prevents the need for costly reassembly and training of a new research team when project grant support is resumed.

At an eastern medical center BRSG funding successfully bridged a financial gap between two NIH research grant periods and extended studies on isolated and separated adrenocortical cells in vitro to the functional level. The results of the studies done during the interim period have been presented at two national meetings.

5) Complements Other Research Funding: In some instances, partial funding for a research project is available from one or more sources, and BRSG funds are used to fill in and unite the pieces into a complete research project.

The National Science Foundation funded a centralized amino acid analyzer facility, which served several institutions. Each institution provides funds for staff and supplies for the first two years of operation. One institution, utilizing the facility for health-related research, used BRSG funds for this purpose. After the initial two years, the facility will be supported by funds from a core of user scientists.

6) Improvement in Research Skills: Obtaining investigators with new skills may become necessary when a research project has to be redirected because of new research findings.

At a northeastern institution BRSG funds were used for the initial costs of securing the special skills of an expert on pulsed, high-frequency nuclear magnetic resonance spectrometry. This expert joined a team of scientists to develop a new complex instrument system that will apply highly advanced knowledge of physics to the understanding of the fundamental molecular basis of human disease.

FISCAL YEAR 1981
ANNUAL REPORT
MINORITY BIOMEDICAL SUPPORT PROGRAM
DIVISION OF RESEARCH RESOURCES

GENERAL RESPONSIBILITY

The Minority Biomedical Support (MBS) Program is charged with the responsibility of trying to rectify the problem of the underrepresentation of ethnic minorities in biomedical sciences. Resolution of this problem is approached through the granting of institutional awards focused on providing minorities equality of opportunity to engage in biomedical research. The MBS Program supports projects designed to strengthen biomedical research capabilities of institutions with a significant commitment to minorities, and to increase and expand the involvement of faculty and students in biomedical research.

SPECIFIC OBJECTIVES

The mission of the MBS Program is to increase the numbers and quality of minority biomedical scientists. This can be accomplished by developing and strengthening the biomedical research setting at minority (eligible) institutions so that the opportunities are expanded for the involvement of ethnic minority faculty and student investigators in biomedical research.

The MBS Program provides funds for released time so that faculty may have the opportunity to conduct biomedically oriented research. Equipment, supplies and necessary renovations for approved research projects are supported by this Program. Funds are also provided for student participation in research. Consortia, collaborative arrangements, special summer projects, and travel to scientific meetings are other activities supported by the program.

In June 1974, the Director of the National Institutes of Health requested that all Bureaus, Institutes and Divisions initiate and coordinate their minority program activities through the existing minority programs (i.e., Minority Access to Research Careers Program (MARC), (NIGMS), and the MBS Program, (DRR). It is through this mechanism that the Co-funding Agreements between the Institutes and the MBS Program were forged. Co-funding Agreements provide for the transfer of funds from one Institute to another for the purpose of supporting elements in the programs of the awarding unit. In this manner, the Institutes' at NIH can identify MBS subprojects that fit within the scope of their mission and funds are transferred to DRR for support of the projects through the MBS grants.

Growth and Scope of the Program

The Program awarded the first grants to 38 institutions in 1972 with a budget of $2 million. The number of grantees has increased to 82 in 1981 with an appropriation of $18.8 million.

The grantee institutions had been subsidizing the indirect costs until Fiscal Year 1979 when the Congress approved and appropriated funds for payment of indirect costs. Therefore, since 1979, the appropriation has included an additional $3-4 milion for indirect costs.

Currently, the MBS Program is serving the minority community through 3 grants that serve primarily American Indians, 47 serving primarily Blacks, four serving primarily Puerto Ricans in Puerto Rico, two in Hawaii and the remainder, serving a mixed population of minorities in the large metropolitan areas and the southwest. This year three new grants were awarded to schools in Colorado, Missouri and Tennessee.

With the initiation of a new computer program MBS is able to immediately access information on Intra-agency and Co-funding Agreements. The DRR system will ultimately interact with the IMPAC System and provide information on each subproject such as the name of the investigator, the project title and direct and indirect costs for the current and future years of support. A computer printout is periodically sent to each BID to keep them informed of ongoing and future commitments. The level of intra-agency co-funding has increased from $340,000 in 1975 when 8 subprojects were supported to $6.04 million in FY 1980 when 145 subprojects received support through other BID's. During FY 1981, a total of 156 projects were supported at a level of $6.42 million. The Environmental Health Sciences Institute has indicated interest in joining 9 other Institutes at NIH and the NIMH to co-fund some of the subprojects in MBS grants. This will expand the opportunities for MBS investigators interested in research relevant to environmental health problems.

ADMINISTRATIVE ACTIONS

Review Procedures

A new review procedure was introduced this year in order to improve the review of individual subprojects and reduce the workload of staff and committee members. Instead of conducting site visits to review a number of supplemental applications, panels, established along disciplinary lines, were set up at NIH to review various subprojects. Each subproject was reviewed separately and assigned a priority score on the basis of scientific merit. The Initial Review Group then reviewed the entire application from each applicant for its total merit and relevance to MBS goals.

A subcommittee of the IRG will review the results of this procedure and consider the more useful and applicable features of the panel procedures to be incorporated into the total review package of the program.

Program Evaluation

A plan for evaluation of the program in FY 1982 was developed during FY 1981. A draft of the plan, identifying the specific objectives and the criteria to be used as measures for evaluation, was developed at a workshop during the annual Program Directors' Meeting. This plan developed with the help of the constituency was reviewed by the Advisory Committee and Council.

A Program Performance Summary was prepared from the plan and submitted to the Associate Director for Program Planning and Evaluation, NIH.

Policy Amendments

For the past two years the staff and reviewers have identified needs relative to policies or guidelines relative to supplemental applications and the level of support for investigators who have other sources of research support. A set of amendments to the Policy and Information Statement was developed and approved by the Advisory Committee and Council. Guidelines to applicants and reviewers concerning the appropriate release time support through the MBS Program were also discussed and agreed upon.

COLLABORATIVE ACTIVITIES WITH OTHER DRR PROGRAMS

In FY 1980, an agreement was established between the MBS Program and the Biotechnology Branch whereby MBS grantees could and did become users of the PROPHET system. The PROPHET system is a highly integrated collection of powerful computer-based tools for the organization, manipulation, analysis, and communication of research data and related information. PROPHET's capabilities are packaged in convenient, easy-to-use form and made available nationwide via a telecommunication network and remote graphic display terminals. PROPHET exists to facilitate laboratory and clinical investigations concerned with how chemical substances influence--and are influenced by--life processes. There are now PROPHET sites at five MBS institutions involving about 110 faculty and student users. The system has opened up a new world of opportunities and experiences for this group of investigators. It has also brought investigators from prestigious institutions in touch with this new pool of student investigators.

A second collaborative effort between the MBS Program and the General Clinical Research Centers Program resulted in an application from Meharry Medical College for a grant to develop clinical research capabilities of Meharry Medical School. This was approved and funded through the MBS Program with the GCRC participating through a Co-funding Agreement.

ACCOMPLISHMENTS

Student Participants

A total of 975 undergraduate students participated in the program in FY 1981. All of the Progress Reports for FY 1980 have not been received but the data available from 62 grantees shows that 499 MBS students received the B.S. degree. Their career choices after graduation led them to: medical school, 129; dental school, 24; graduate school, 137; and other health related schools, 115. This year 80% of the MBS graduates from the four junior colleges in the program transferred to four-year schools to continue their training in biomedical areas.

The graduate student participation in the program for FY 1981 numbered 368. An estimated ten of these completed the Ph.D. and 90 completed the M.S. degree. About 400 students presented papers at the Annual MBS Symposium held in Albuquerque this year. About 40 MBS students spent the summer in research participation at NIH laboratories. These students were sponsored by the Allergy and Infectious Diseases Institute, the Cancer Institute, the Heart Lung and Blood Institute, and the Neurology Institute.

Faculty Investigators

A total of 636 faculty participated in 507 projects in FY 1981. No data are available yet for FY 1981 on accomplishments, but 63 grantee reports for FY 1980 show that there was a significant amount of research accomplished. There were 305 scientific papers published and 757 presentations made at scientific meetings in 1980. Several more MBS faculty have been nominated to NIH advisory and review committees to augment or replace the 30 that were members last year.

The quality of science at MBS supported institutions and the reputations of MBS investigators have continued to increase. Examples of the research efforts are the following:

> An investigator in the Department of Natural Sciences at Medgar Evers College and collaborators at the Albert Einstein College of Medicine have been the first to demonstrate that there are drug binding sites in the pedal ganglia of the marine mollusc Mytilus edulis. The nervous system of this invertebrate is considerably less complicated than mammalian systems but is a good model for monitoring cellular and electrical changes induced by drugs. The investigator chaired a session and reported on his research at the XVIII International Congress of Physiological Sciences in Budapest, Hungary in July 1980. He plans to present new research findings at the International Congress on Comparative Neuropharmacology to be held in Japan in 1981.
>
> Investigators at Bishop College, an undergraduate institution in Dallas, have developed a rapid (four minute) procedure using ^{125}I to qualitatively and quantitatively determine the molecular weight of RNA samples. This rapid iodination procedure, when combined with two-dimensional gel electrophoresis, simplifies identification of RNA without interference from impurities.
>
> At Howard University, an investigator is carrying out research on breast tumor growth. By studying mammary cancer induced in laboratory rats by a carcinogenic agent, he is beginning to delineate the role of hormones and certain hormone inhibitors on the rate of tumor growth. Approximately 40 percent of the mammary carcinoma occurring in American women appears to be hormone dependent. Recently, it was demonstrated in this laboratory that the compound CI-628, a female hormone antagonist, which competively binds to hormone receptors, induces tumor regression and terminates the synthesis of an important

catalyst in tumor cells. It was also shown that another female hormone antagonist, progesterone, results in a blockage of the biological processes involved in tumor development.

Anti-inflammatory steroids are being developed by researchers in the College of Pharmacy at Florida A&M University in Tallahassee. Studies in rats indicate that two new compounds have a marked local anti-inflammatory action without any of the usual toxic effects caused by the corticosteroids currently employed for topical application.

Biologists at the University of Puerto Rico, Rio Piedras campus, are developing a vaccine against schistosomiasis, a parasitic disease which affects 10 to 15 percent of Puerto Ricans and over 200 million people in tropical areas throughout the world. Tests of a new vaccine, isolated from a related parasite, Fasciola hepatica, which infects the livers of cattle and sheep, gave a significantly higher degree of protection than has been obtained using other methods. Efforts are continuing to improve the vaccine to achieve at least 80% protection consistently, to identify all the protective antigens and optimize treatment regimens and, eventually, to test the vaccine in non-human primates.

MBS investigators at the University of Maryland, Eastern Shore, have been studying marine algae in order to isolate medically active compounds (bioactive compounds from natural sources include digitalis, reserpine, atropine and colchicine). They are studying a species of marine "red-tide" dinoflagellates which produce some of the most potent toxins known to man. The study of the toxins is important not only for the potential of obtaining new compounds for the treatment of disease, but also for the development of an effective treatment for human or animal intoxication from venoms of toxic marine organisms. The team has been successful in culturing large volumes of cells under conditions which promote high toxin production, and has improved techniques for harvesting and purifying the toxic material so that physiological, pharmacological and toxicological studies can be carried out without delays due to unpredictable toxin supplies.

The Annual MBS Symposium

The symposium, held in Albuquerque, New Mexico, attracted about 1,500 participants. Among the highlights were 272 papers and 212 posters presented by student and faculty investigators. Three mini symposia were also conducted. The symposia topics were; "Endorphins: Natural Pain Killers", "The Fetal Alcohol Syndrome" and "Recent Advances in Cancer Research." A workshop on grantsmanship was also conducted by NIH staff and some members of NIH review committees.

Invited speaker U.S. Senator Harrison Schmidt talked about the experiences that led him to become a scientist astronaut who visited the moon and then turned to politics. The informative lecture given by Congressman Manuel

Lujan of New Mexico described the process by which an idea becomes a bill in Congress and how that bill is enacted into a law. The George Willis Memorial lecture featured Dr. John Baxter in a presentation, "Application of Recombinant DNA Technology".

MBS Resource Development Highlights

A 3-year grant to Howard University, College of Medicine has just been completed. This non-renewable support, limited to one three-year period, has assisted them in developing their research capability in cellular and molecular biology has been completed. They are now competing for regular research grants and are productively engaged in state-of-the-art biomedical research and research training.

A similar situation has developed at the Atlanta University Center involving a consortium of 5 institutions. These institutions, prior to the MBS Program, did not have significant biomedical research capabilities and especially did not have access to centrally-shared research resources. The MBS Program has provided the funds so that in the past year they have been able to establish a complete electron microscopy resource for transmission and scanning electron microscopy with computerized capability. They have also been able to complete their centrally-shared instrumentation resource for biochemistry and molecular biology research. This latter resource involves high resolution spectrometry of various sorts and a computer facility that includes a hookup with the PROPHET System of DRR. Completion of these resources is beginning to payoff with productivity in state-of-the-art biomedical research and research training. The scientists are now able to compete for research support with scientists at the more prestigious and established universities.

In Puerto Rico, at the Rio Piedras Campus, University of Puerto Rico, there is now a very productive laboratory of immunology established and developed by the MBS Program. The investigator is considered an authority on immunological research and his laboratory is a pioneer in immunodiagnosis, having published 21 papers on this topic in the last three years.

At Incarnate Word College, San Antonio, Texas, 148 students have participated in the MBS Program since 1973. Twenty-two have been awarded the M.D. at various medical schools; twenty-eight are presently enrolled in medical school; seven have been awarded the D.D.S.; eleven are currently enrolled in dental school; fourteen have been awarded the M.S. degree; ten are currently enrolled in graduate school (four Ph.D. candidates), and twenty-six are employed in health related fields.

OFFICE OF GRANTS AND CONTRACTS MANAGEMENT

The Office of Grants and Contracts Management (OGCM) continues to play an important role in the review, negotiation, award making, and the administration of the Division grant programs, as well as aiding in the administration of contracts that are made by the Research Contracts Branch, Division of Contracts and Grants. During FY 1981, a total of 1,090 grant awards in the amount of $173,880,000, and 20 contract modifications and 2 intra-agency agreements in the amount of $4,515,000 were made.

There were a number of revised awards that had to be made because of the uncertainty of FY 1981 funding of DRR Programs. This created an additional work load for OGCM as well as uncertainties and confusion for the grantee community. OGCM developed a new funding mechanism called "Co-Funding". Co-Funding allows the various NIH Institutes to directly co-fund an award along with the awarding Institute or Division that administers the grant. Co-Funding was used for funding the FY 1981 Minority Biomedical Support (MBS) grant program as an NIH trial for this mechanism. A total of $5,554,587 through Co-Funding was provided by the various NIH Institutes, and $923,000 was received from NIMH through an intra-agency agreement for a total of $6,477,587. OGCM conducted an educational program with the various NIH Institutes on how the Co-Funding mechanism works. It is believed that in the future it is a tool that will be used throughout NIH.

The following tables and charts reflect the total DRR grant and contract effort for FY 1981. Particular attention is invited to the chart titled "Division of Research Resources Research Grant Award in Current & Constant Dollars Fiscal Years 1971 - 1981." It should be noted that for the past two years there has been a very slight upward trend of constant dollars compared to current dollars.

DIVISION OF RESEARCH RESOURCES
FY 1981 OVERVIEW OF GRANT AND R&D CONTRACT PROGRAMS

Program	Funding	Major Resources Supported
General Clinical Research Centers Program	$ 60,148,000	• 75 General Clinical Research Centers (Includes two phase outs) • Over 3200 Research Projects • 40 Clinical Associate Physicians • 2 Contracts
Biotechnology Resources Program	$ 19,642,000 1/	• 48 Biotechnology Resources — 17 Computer Resources (3 contracts) — 3 Biomedical Engineering Resources — 24 Instruments for Biological Structure and Function — 1 Cellular and Biochemical Material Resource
Animal Resources Program	$ 25,052,000 2/	• 7 Primate Research Centers, including 220 Core Research Projects • 7 Primate Breeding Projects • 60 Animal Research and Resource Project Grants and Contracts • 8 Training Programs
Minority Biomedical Support Program	$ 25,330,000 3/	• 80 Institutions • 507 Research Projects • 636 Faculty, 975 Undergraduates, and 368 Graduate Students • 5 Prophet Sites • Minority Symposium
Biomedical Research Support Program	$ 47,146,000	• Biomedical Research Support Grants to 527 Institutions • 10,000 Pilot Research/Regular Research Projects • Central Resources • Development Awards to 19 Institutions • Minority High School Research Apprentice Awards for 1219 Students
Office of the Director	$ 1,077,000 4/	• Culture Collection and Research Resources Reporter Contracts
Total Funding	$178,395,000	

1/ Includes $ 734,000 other than DRR appropriated funds
2/ Includes 46,000 " " " " "
3/ Includes 6,478,000 " " " " "
4/ Includes 590,000 " " " " "
$ 7,848,000

OGCM FY-1981

DRR FY 1981 GRANT AND R&D CONTRACT AWARDS BY MECHANISM

(Dollars in Thousands)

PROGRAM ACTIVITY	Research Grants: Research Centers Type	No.	Amount	Research Grants: Other Research Type	No.	Amount	Training Programs Type	No.	Amount	Res. & Develop. Contracts Type	No.	Amount
General Clinical Research Centers Program..........		M01s			P09s							
	2	18	$14,168	3	1	$ 200				New		--
	3	19	718							Mod.	2	$ 40
	5	58	45,022									
		95	$59,908									
Biotechnology Resources Program..................		P41s			P09s							
	1	3	$ 767	3	1	$ 84				New		--
	2	8	4,491		R01s					Mod.	8	$2,651
	3	11	1,882	3	1	$ 25				Intra-Agency		84
	5	25	8,728		R13s							$2,735 1/
		47	$15,868	1	3	$ 42						
					R23s							
				1	1	$ 56						
					R24s							
				2	1	$ 322						
				5	2	510						
					3	$ 832						
Laboratory Animal Sciences and Primate Research Program..................		P40s			P09s			F32s				
	1	5	$ 681	3	1	$ 120	1	1	$ 19	Mod.	8	$ 502
	2	8	1,219							Intra-Agency		61
	3	6	202		R24s			T32s				$ 563
	5	27	3,726	2	2	$ 287	5	8	$ 575			
		46	$ 5,828	3	1	2						
				5	7	428						
		P51s			10	$ 717		T35s				
	2	2	$ 4,537				5	1	$ 13			
	3	2	2,814									
	5	4	9,866									
		8	$17,217 2/									

OGCM FY-1981

DRR FY 1981 GRANT AND R&D CONTRACT AWARDS BY MECHANISM (CONTD)

(Dollars in Thousands)

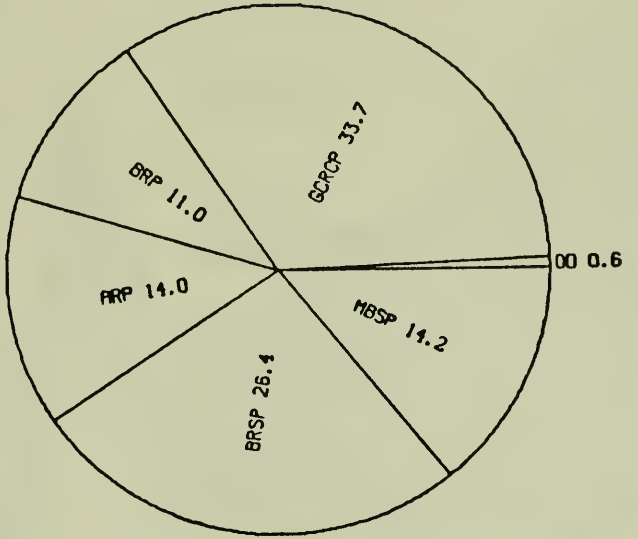
PROGRAM ACTIVITY	Research Grants: Research Centers Type	No.	Amount	Research Grants: Other Research Type	No.	Amount	Training Programs Type	No.	Amount	Res. & Develop. Contracts Type	No.	Amount
Biomedical Research Support Program...........					P09s							
				3	1	$ 18						
					S03s							
				1	230	$ 999						
					S07s							
				1	24	$ 768						
				2	503	43,808						
					527	$44,576						
					S08s							
				5	19	$ 1,553						
Minority Biomedical Support Program...........					P09s							
				3	1	$ 200				Mod.	1	$ 100 6/
					R13s							
				5	1	$ 62						
					S06s							
				1	3	1,230						
				2	19	6,497						
				3	9	615						
				5	57	16,626						
					88	$24,968 5/						
Office of the Director....										New Mod	 2	-- $1,077 4/
TOTAL		196	$98,821		884 5/	$74,452		10	$ 607		20	$4,515

1/ Includes $ 734 other than DRR appropriated funds
2/ " 46 " " " " "
3/ " 6,478 " " " " "
4/ " 590 " " " " "
$7,848

5/ Each DRR Program contributed to Scientific Evaluation Grant (P09). Counted only as one grant under the Biotechnology Branch.

6/ Used to support Prophet. Count included in Biotechnology contract number.

DIVISION OF RESEARCH RESOURCES
FY 81 AWARDS BY COMPONENT
Research Grants, Research Training, and R&D Contracts



OGCM FY-1981

DIVISION OF RESEARCH RESOURCES

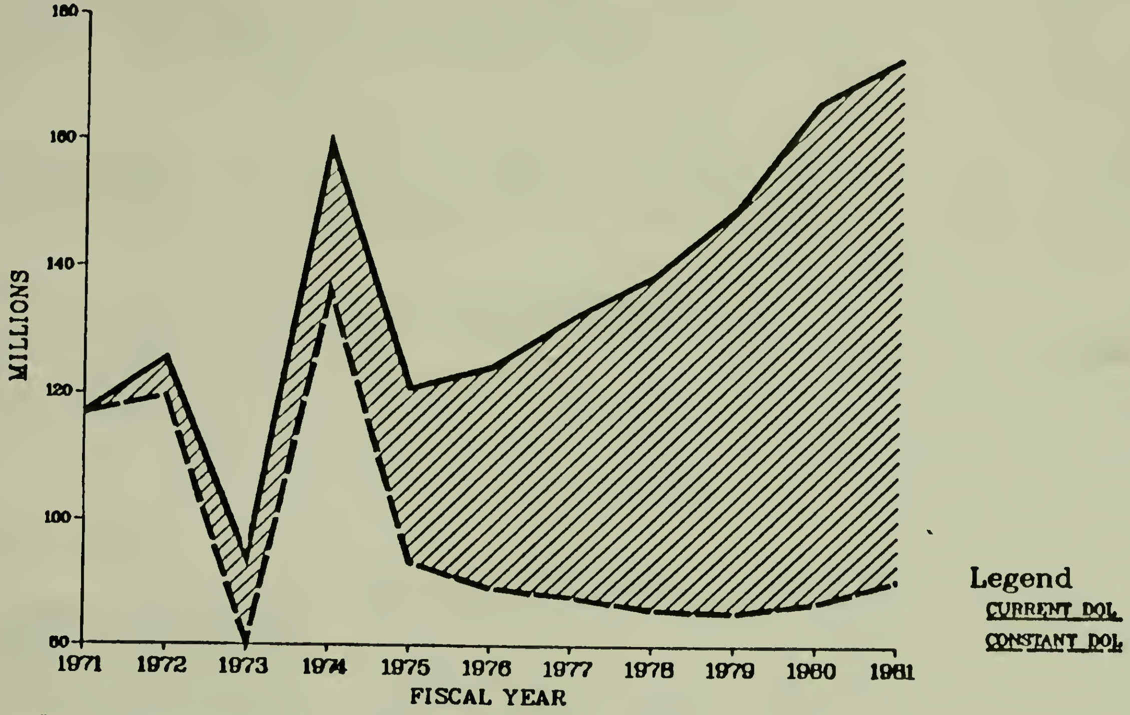
FY 81 AWARDS BY COMPONENT

Research Grants, Research Training, and R&D Contracts

General Clinical Research Centers Program	Research Centers	$ 59,908,000	
	Other Research	200,000	
	Contracts	40,000	
		$ 60,148,000	(33.7%)
Biotechnology Resources Program	Research Centers	$ 15,868,000	
	Other Research	1,039,000	
	Contracts	2,735,000	
		$ 19,642,000	(11.0%)
Animal Resources Program	Research Centers	$ 23,045,000 1/	
	Other Research	837,000	
	Training	607,000	
	Contracts	563,000	
		$ 25,052,000	(14.1%)
Minority Biomedical Support Program	Other Research	$ 25,216,000	
	Contracts	100,000	
		$ 25,330,000	(14.2%)
Biomedical Research Support Program	Other Research	$ 47,146,000	(26.4%)
Office of the Director	Contracts	$ 1,077,000	(.6%)
		$178,395,000	(100%)

1/ $17,217,000 of this amount was for Primate Centers.

DIVISION OF RESEARCH RESOURCES
Research Grant Award in Current & Constant Dollars
FISCAL YEARS 1971 – 1981



NOTE: CONSTANT DOLLARS BASED ON BIOMEDICAL R&D PRICE DEFLECTOR FY 1971 = 100

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SOURCE: BASIC DATA BOOKS FY 71-81, NIH, PHS, DHHS

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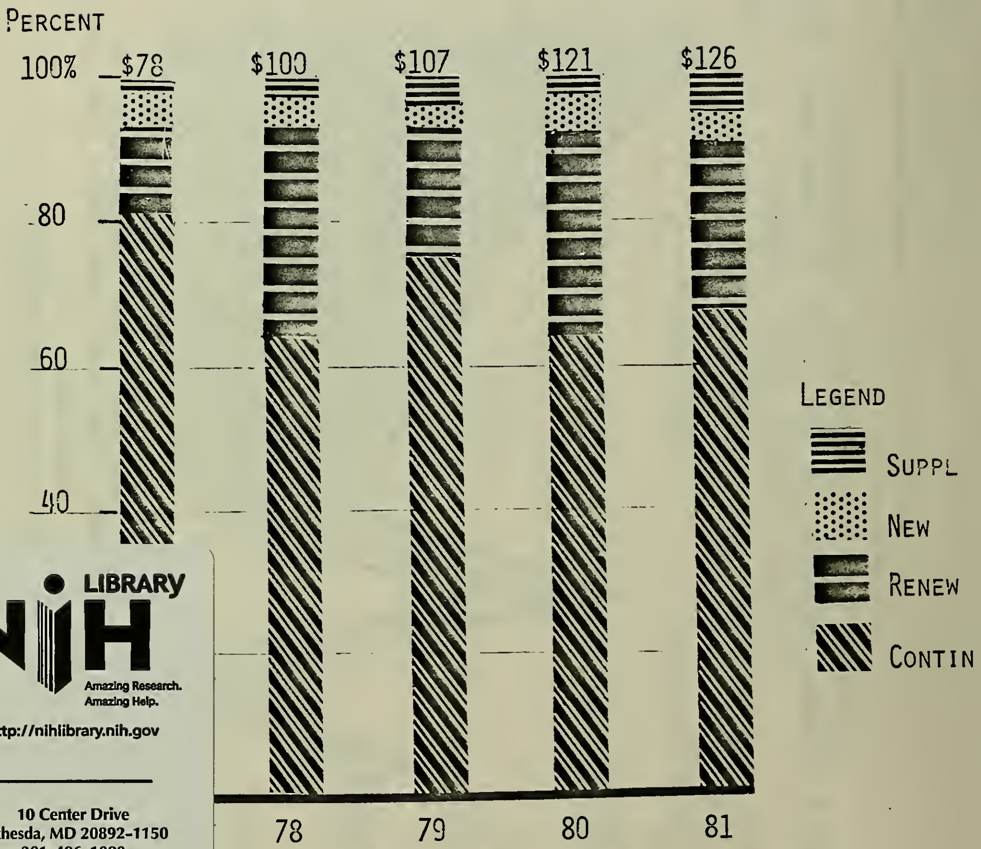
DRR RESEARCH GRANTS BY TYPE
FISCAL YEARS 1977-1981

(PERCENT OF AMOUNT AWARDED; DOLLARS IN MILLIONS)



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ES BRS AWARDS

DATA: NIH, DRG, STATISTICS & ANALYSIS BRANCH

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